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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of:	Pramod K. Srivastava	Confirmation No.:	4225
Serial No.:	09/090,754	Art Unit:	1642
Filed:	June 4, 1998	Examiner:	Anthony C. Caputa
For:	COMPOSITIONS AND METHODS FOR THE PREVENTION AND TREATMENT OF PRIMARY AND METASTATIC NEOPLASTIC DISEASES WITH HEAT SHOCK/STRESS PROTEINS	Attorney Docket No:	8449-041

REQUEST UNDER 37 C.F.R. § 41.202(a)
FOR INTERFERENCE WITH PATENT NO. 6,713,608 B2

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

Pursuant to 37 C.F.R. §41.202(a), Applicant (hereafter "Fordham") [1] requests an interference between the above-captioned application and Patent No. 6,713,608 B2 (" '608 patent") (Exhibit 1) of Wallen *et al.*, entitled "Purified Heat Shock Protein Complexes." The '608 patent issued March 30, 2004, from application Serial No. 10/176,418 (" '418 application"), filed June 20, 2002, and is assigned on its face to Science & Technology Corporation @ UNM.[2]

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[1] The above-captioned application is assigned to Fordham University. Accordingly, in regard to the above-captioned application, reference will be made to party "Fordham," to be consistent with the terminology used in prior Interference 104,761, which involved the above-captioned application.

[2] Science & Technology Corporation @ UNM is a nonprofit corporation formed and owned by the University of New Mexico (Exhibit 6). For the purposes of this Request, it has been assumed that the real party in interest with respect to the '608 patent is, ultimately, the University of New Mexico. For convenience, party Fordham will also use the term "UNM," to encompass the inventors, the attorneys or agents involved in the preparation and/or prosecution of either or both of the '381 application and the '418 application, as well as those involved in Interference 104,761, and every other individual who was substantively involved in these matters and who was associated with the inventors or the assignee.

Attached as Exhibit 2 is a listing of Fordham's allowed claims in the above-captioned application.

The effective filing date of UNM's '608 patent is more than a year *later* than the effective filing date of the above-captioned application for the proposed interfering subject matter. Consequently, this Request is properly filed under former 37 C.F.R. § 1.608(a) and current 37 C.F.R. § 41.202 (a)(4), and 37 C.F.R. § 41.202(d).

Although the proposed new interference would involve the same parties (*i.e.* Fordham and UNM) involved in Interference 104,761, the requested interference would not have been precluded under former Rule 665, because it would be declared upon an issued patent, rather than an application, for inventions defined by the counts of Interference 104,761.

This Request proposes three counts ("Fordham Proposed Counts 1-3" *see* Section III, below) that correspond to, but are broader than, Counts 1, 4(2) [3], and 3, respectively, of Interference No. 104,761. Interference 104,761 was initially declared October 12, 2001, between the above-captioned application of party Fordham, and U.S. Patent No. 5,747,332 (Exhibit 3) of the University of New Mexico ("UNM"). This interference was redeclared twice to include two other UNM patents: U.S. Patent No. 6,066,716, and U.S. Patent No. 6,433,141 (Exhibits 4 and 5, respectively).

Pursuant to the final judgment issued in Interference 104,761 (Exhibit 7), the Board ordered:

(1) that UNM was not entitled to a patent containing claims 1, 3-5, 7-13, 15-17, and 19-23 of UNM's U.S. Patent No. 5,747,332;

(2) that UNM was not entitled to a patent containing claims 13-30 of UNM's U.S. Patent No. 6,066,716; and

(3) that UNM was not entitled to a patent containing claims 1-18 of UNM's U.S. Patent No. 6,433,141.

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[3] In Interference 104,761, Fordham filed a preliminary motion to substitute a proposed count 4 for count 2, as originally proposed, in order to eliminate an implicit ordering of steps in the subject method. This motion was granted; accordingly, throughout the present request, reference is made to count 4(2) of Interference 104,761 to reflect this substitution.

UNM's '608 patent should not have been allowed to issue since, under former 37 C.F.R. 1.658, UNM was estopped by the decision in Interference 104,761 that was adverse to UNM. In view of that Decision, Fordham submits that UNM's prosecution of the '418 application and issuance of the claims of the '608 patent effectively undermines the authority of the Board since those activities were in direct contradiction to the principles of *res judicata* and collateral estoppel (*see e.g. In re Deckler* 977 F.2d 1449, 1452, 24 USPQ2d 1448, 1449 (Fed. Cir. 1992)). Each of the three claims of the '608 patent is an independent claim that is patently indistinguishable from UNM's claims involved in Interference 104,761.[4] Moreover, each of the three claims of the '608 patent is patently indistinguishable over Counts 1-3, respectively, of Interference 104,761 (*see* Sections VIII (C) and (D), below). Therefore, denial of this Request would allow an undeserving UNM to circumvent the consequences of its adverse decision in Interference 104,761, and to recapture subject matter it had lost in that interference (*see e.g. In re Kroekel et al.* 803 F.2d 705, 231 USPQ 640, 644 (Fed. Cir. 1986)).

Fordham is the first inventor of the invention encompassed within claims 1-3 of UNM's '608 patent. Interference 104,761 established that Fordham's above-identified application was entitled to benefit of the September 13, 1995 filing date of its parent application Serial No. 08/527,391 for a constructive reduction to practice falling within the scope of each of the three counts of Interference 104,761. Moreover, since the September 13, 1995 date was more than seven months earlier than the earliest date of invention alleged by UNM in its preliminary statement (Exhibit 10), Fordham prevailed on priority in Interference 104,761. Since each of Fordham's disclosed embodiments also falls within the scope of the counts proposed herein, Fordham submits that it will necessarily prevail on priority in an interference between the above captioned-application and UNM's U.S. Patent No. 6,703,608.

UNM's '608 patent should be held unenforceable for inequitable conduct during prosecution of UNM's '418 application. While Interference 104,761 was pending, unbeknownst to Fordham (and presumably the Administrative Patent Judge), UNM filed and prosecuted the '418 application and, despite the now-final decision that was adverse to UNM on all counts, allowed the '608 patent to issue. Furthermore, there is no indication in the file history of UNM's

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[4] The '608 patent was issued with a terminal disclaimer (*see* Exhibit 8) over each of the three patents of UNM that were involved in Interference 104,761. The terminal disclaimer was filed in response to a rejection of the pending claims as not patentably distinct over the claims of UNM's '332, '716, and '141 patents, under the judicially-created doctrine of obviousness-type double patenting.

'418 application that the Examiner was ever notified of pending Interference 104,761 or the decisions reached by the Board in that interference (*see* Section VIII (E), below).

In this request, Fordham will also demonstrate that the inventions of claims 1, 2, and 3 of UNM's '608 patent are unpatentable to UNM. Accordingly, Fordham is *prima facie* entitled to judgment over UNM for that reason alone (*see* Sections VIII (A) and (B), below).

I. BACKGROUND

A. The Parties' Applications

UNM's '608 patent issued March 30, 2004, from application Serial No. 10/176,418 (" '418 application). The '418 application was filed June 20, 2002, as a division of application Serial No. 09/534,381 (" '381 application"). The '381 application was filed on March 24, 2000 as a division of application Serial No. 08/934,139 (" '139 application"), and issued as U.S. Patent No. 6,433,141 (" '141 patent") on August 13, 2002. The '139 application was filed September 19, 1997 as a division of application Serial No. 08/717,239 (" '239 application"), and issued as U.S. Patent No. 6,066,716 (" '716 patent") on May 23, 2000. The '239 application was filed on September 20, 1996, and issued as U.S. Patent No. 5,747,332 (" '332 patent") on May 5, 1998.

Fordham's above-captioned application Serial No. 09/090,754 (" '754 application") (Exhibit 9) was filed June 4, 1998 and claims priority under 35 U.S.C. § 120 as a continuation of application Serial No. 08/527,391 (" '391 application"). The '391 application was filed September 13, 1995, and issued November 17, 1998, as U.S. Patent No. 5,837,251 (" '251 patent").

As demonstrated below and as established in prior Interference 104,761, Fordham is entitled to benefit of the September 13, 1995 filing date of its earlier-filed '391 application for a constructive reduction to practice falling within the scope of each of Fordham Proposed Counts 1-3.

UNM's '608 patent should, at best, be accorded benefit of the September 20, 1996

filing date of UNM's '239 application.[5] Thus, Fordham's effective filing date is more than one year *prior* to the effective filing date of UNM's '608 patent for the subject matter of each of Fordham Proposed Counts 1-3.[6]

B. The Interfering Subject Matter

(1) The Specification of UNM's '608 Patent

In the section entitled Background of the Invention (column 1, line 15 through column 2, line 4), the '608 patent summarizes prior art publications [7] that disclose the utility of non-covalent heat shock protein (hsp) -peptide complexes for the treatment and prevention of infectious disease and cancer. These references suggest that the immunogenicity of the hsp-peptide complexes apparently might be attributed to the immunogenicity of the non-covalently-bound peptides.

The cited art also disclosed that isolation methods that employed an ATP-agarose column appeared to provide purified heat shock proteins *per se* rather than hsp-peptide complexes. This observation established that there was a need in the art for methods for the isolation and for the synthesis of hsp-peptide complexes.

UNM's '608 patent provides a description of the claimed methods for purification and synthesis of heat shock protein complexes in both the Summary of the Invention (at column 2, lines 6-35) as well as in the Detailed Description of the Preferred Embodiment (from column 2, line 48 through column 3, line 58).

Subsequently, at column 3, lines 59-63, UNM's '608 patent further provides:

Although there are many heat shock proteins that <u>may</u> be used in the method of

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[5] This statement should not be construed as an admission that UNM is entitled to the benefit of *any* "parent" application of the '608 patent. As demonstrated in Section VIII of this Request, the claimed subject matter of UNM's '608 patent is unpatentable to UNM, and, therefore, UNM is not entitled to any date of invention for that subject matter.

[6] Moreover, as established in prior Interference 104,761, UNM's earliest asserted date of conception of the subject matter of the counts in that interference, was April 22, 1996, which is more than seven months *after* Fordham's effective filing date for the above-captioned application (UNM Preliminary Statement; Exhibit 10; note that all documents in Interference 104,761 were filed and served electronically; accordingly those documents were not signed by hand).

[7] This "Description of the Prior Art" section of the '608 patent cites ten publications, eight of which include the above-captioned inventor as the sole author or as a co-author.

> the present invention, heat shock proteins that have proven particularly useful include members of the hsp60 family, hsp70 family, hsp90 family and the hsp104-105 family (emphasis added).

The four paragraphs that follow (from column 3, line 64 through column 4, line 11 of UNM's '608 patent) provide a listing of hsp species, all of which were known in the art. This listing included heat shock proteins that had been classified as falling within the hsp60, hsp70, hsp90, and the [alleged] hsp104-105 families of heat shock proteins.

For example, the hsp70 family includes the species designated "eukaryotic hsp70," which is the heat shock protein present in the complexes isolated in Example 1 of UNM's '608 patent (*see e.g.* column 4, lines 2-6). Example 1 and Figure 1 of UNM's '608 patent demonstrate the isolation of hsp70-peptide complexes from mammalian cells using an ADP-agarose column. Example 2, in conjunction with Figures 2 and 3, demonstrates that exposure of such complexes to ATP results in the release of non-covalently-bound peptides (a result that was noted, at column 5, lines 4-7 of UNM's '608 patent, to be consistent with data published in an article from laboratory of Dr. Srivastava (the inventor of the above-captioned application)).

(2) Construction of the Phrase: "Non-hsp70 heat shock protein"

The recited genus of claims 1-3 of UNM's '608 patent only exclude the heat shock protein species, hsp70. Each of the claims of UNM's '608 patent includes, as a negative limitation, the proviso that the recited complexes are "non-hsp70 heat shock protein" complexes. The terms "hsp60," "hsp70," and "hsp90," in isolation, can be ambiguous. Each of these terms is descriptive of both an identified family of heat shock proteins as well as a specific member of that family. Such potential ambiguity is avoided, for example, by using the phrases "hsp70 family," "hsp60 family," and "hsp90 family" when the referring to the entire family of related proteins, and the terms "hsp60," "hsp70," and "hsp90", when referring to the particular species. This is the practice adopted in the specification of UNM's '608 patent (*see e.g.* column 3, line 59 through column 4, line 8 of UNM's '608 patent). According to this convention, then, absent any additional information, the plain meaning of "hsp70" is the specific eukaryotic protein, hsp70, and the plain meaning of the phrase "hsp70 family" is the entire set of related proteins (*see e.g.* UNM's '608 patent at column 3, lines 62-64).

In view of UNM's adherence to this convention, it is clear that had UNM intended a negative limitation excluding all members of the hsp70 family, it would have done so explicitly by reciting "hsp70 family." Therefore, it is Fordham's position that claims 1 and 2 of UNM's '608 patent are unambiguously directed toward methods for the purification and the synthesis, respectively, of a genus of hsp complexes, where those complexes include any heat shock protein other than the species, hsp70.

Similarly, it is Fordham's position that claim 3 of UNM's '608 patent is directed toward a genus of ternary complexes, in which each member of that genus is a complex of ADP, a peptide, and any heat shock protein other than the hsp species, hsp70.

Accordingly, the genus recited in each of the claims of UNM's '608 patent encompasses complexes in which the hsp is selected from a group that includes, *inter alia*, DnaK, Ssa, Ssb, Ssc, Grp75, and Grp78(BiP), *i.e.* a group that includes all members of the hsp70 family of heat shock proteins other than the specifically-excluded species, hsp70.

II. AN INTERFERENCE-IN-FACT EXISTS BETWEEN CLAIMS 1-3 OF UNM'S '608 PATENT AND ALLOWED CLAIMS 62, 65, AND 68 OF FORDHAM'S ABOVE-CAPTIONED APPLICATION

Former 37 CFR § 1.601(j) provided that:

> "[a]n interference-in-fact exists when at least one claim of a party that is designated as corresponding to a count and at least one claim of an opponent that is designated to correspond to the count define the same patentable invention."

The phrase "same patentable invention," in turn, was defined by 37 CFR § 1.601(n) as follows:

> Invention "A" is the same patentable invention as an invention "B" when invention "A" is the same as (35 U.S.C. 102) or is obvious (35 U.S.C. 103) in view of invention "B" assuming invention "B" is prior art with respect to invention "A."

New Board Rule 203(a) (*Interfering Subject Matter*) provides that

> An interference exists if the subject matter of a claim of one party would, if prior art, have anticipated or rendered obvious the subject matter of a

claim of the opposing party, and vice versa.

Therefore, determination of whether an interference-in-fact exists relies upon a two-way patentability analysis in which each of the subject inventions is, in turn, deemed to be prior art to the other (*see* 69 FR 155, at page 49969, left column, seventh full paragraph). If, in both instances, both inventions would be anticipated by or be obvious over the other in view of the art, where the other is deemed to be part of that prior art, then the claims are directed toward interfering subject matter and an interference-in-fact between the inventions has been established *Winter v. Fujita*, 1999 WL 1327616, 53 USPQ2d 1234, 1243 (BPAI 1999); *Eli Lilly & Co. v Board of Regents of the University of Washington*, 334 F.3d 1264, 1268, 67 USPQ2d 1161, 1164 (Fed. Cir. 2003).

For the reasons provided below, Claims 1-3 of UNM's '608 patent define the same patentable invention as claims 62, 65, and 68 of Fordham's above-captioned '754 application. Accordingly, an interference-in-fact exists between Fordham's allowed claims 62, 65, and 68 of the above-captioned application and claims 1-3, respectively, of UNM's '608 patent since the respective claims are directed toward interfering subject matter (37 C.F.R. § 41.203 (a)).

A claim is anticipated under 35 U.S.C. § 102, if a single prior art reference discloses each and every limitation of that claim, either expressly or inherently (*see e.g. Verdegaal Bros. v. Union Oil Co. of California* 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987)). Disclosure of single species falling within the scope of a claimed genus will anticipate that generic claim (*see e.g. In re Gosteli* 872 F.2d 1008, 1010, 10 USPQ2d 1614, 1616 (Fed. Cir. 1989)).

An invention is obvious under 35 U.S.C. § 103(a), if the "differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art." (*In re Dembiczak*, 175 F.3d 994, 998, 50 USPQ2d 1614, 1616 (Fed. Cir. 1999)). Relevant factual inquiries underlying the legal conclusion of obviousness include an evaluation of the scope and content of the prior art, the level of skill in the art, and the differences between the prior art and the claimed invention (*Id.*). Accordingly, the legal standard of *prima facie* obviousness requires that three criteria be met: (1) the prior art, either alone or combination,

must teach or suggest each and every limitation; (2) there must be a suggestion or motivation in the cited references or in the art to modify or combine the cited references; and (3) the cited references must provide a reasonable expectation of successfully achieving the claimed invention. *In re Vaeck*, 947 F.2d 488, 493, 20 USPQ2d 1438, 1442 (Fed. Cir. 1991); *In re* Wilson, 424 F.2d 1382, 1384, 165 USPQ 494, 496 (CCPA 1970).

In the present instance, relevant prior art includes that related to the properties of heat shock protein families in general, to specific traits and properties of individual heat shock proteins that are conserved across family "boundaries," to existing methods for isolation of hsp-peptide complexes, as well as to that art concerning general principles of chromatographic separation of proteins. In light of this art, it is clear that the methods of purification and synthesis of hsp-peptide complexes, as well as the complexes *per se*, that are recited in claims 1-3 of UNM's '608 patent and Fordham independent claims 62, 65, and 68, respectively, would each be anticipated by or be obvious over the other, where the other was deemed to be prior art.

A. The Prior Art

The four sections that follow present salient disclosures of the prior art concerning (i) the general features of the heat shock protein "superfamily," (ii) specific biochemical properties shared among members of the heat shock protein superfamily, (iii) the utility of heat shock protein - peptide complexes, and (iv) the properties of (three) well-characterized heat shock proteins, (hsp70, hsp90, and gp96/grp94 (gp96 and grp94 are the same protein: *see* Section II(A)(4)(a), below)) that are representative of the hsp70 and hsp90 families of heat shock proteins.

(1) Heat Shock Proteins

Heat shock proteins, which include those polypeptides synthesized by an organism in response to heat, and/or other physiological stress, are among the most highly conserved proteins in existence (Lindquist (1988) "The Heat Shock Proteins," *Ann. Rev. Genet.* 22: 631-637 ("Lindquist") (Exhibit 11), at page 632, lines 1-9). Heat shock proteins have also been referred to as protein chaperones based upon their ability to bind to partially folded proteins and facilitate their correct folding. Chaperones are generally members of, for example, the hsp60, hsp70, and the hsp90 families of heat shock proteins (Gething (1992) *Nature* 355: 33-45

("Gething") (Exhibit 12) at page 35, left column, last paragraph, lines 1-5), and include the species recited in the specification of the '608 patent at column 4, line 59 through column 5, line 11. Although chaperones perform many different roles in various cells and organelles, each of these functions involves the conserved ability of heat shock proteins to interact with proteins and modulate their folding (Gething (Exhibit 12), at page 35, right column, first full paragraph, lines 1-3 and Table 2, at page 37).

Therefore, it was well known in the art that even though different heat shock protein species performed different, defined roles, these specific cellular functions were simply variations on a fundamental theme reflecting the universal ability of heat shock proteins to bind to peptide sequences.

(2) Specific Traits and Properties of Individual Heat Shock Proteins That Are Conserved Across Family Boundaries

Although many different heat shock protein species have been identified (*e.g.* Tables 1 and 2 in Gething (Exhibit 12) at pages 35 and 37 respectively), they share two specific traits that are highly conserved among heat shock proteins. This is true even when such proteins are viewed collectively as a "superfamily" encompassing, *e.g.* the hsp60, hsp70, and hsp90 protein families. These conserved traits are: (1) the ability to bind adenine ribonucleotides and (2) the ability to bind peptides. For example, although GroEL (hsp60 family member) and DnaK (hsp70 family member) do not have significant amino acid sequence homology, it was readily demonstrated that both of these proteins bind to the same protein ligand immobilized on a Sepharose matrix and both can be eluted from that matrix with ATP (Sherman (1991), "Formation In Vitro of Complexes Between an Abnormal Fusion Protein and the Heat Shock Proteins from *Escherichia coli* and Yeast Mitochondria," *J. Bacteriol.* 173(22): 7249-7656 ("Sherman") (Exhibit 13), at page 7249, Abstract, lines 2-11).

Similarly, gp96, a representative member of the hsp90 family of proteins, had been shown to bind ATP and to bind peptides (Li (1993) "Tumor Rejection Antigen gp95/grp94 is an ATPase: Implications for Protein Folding and Antigen Presentation," *EMBO J.* 12(8): 3143-51 ("Li") (Exhibit 14) at page 3143 Abstract, lines 13-17). In fact, under the experimental conditions employed, it was possible to immunoprecipitate populations of hsp70 and gp96 which comprised hsp70-ADP and gp96-ADP complexes (Li (Exhibit 14) FIG. 3B at page 3145).

Moreover, hsp90 has been reported to associate with a "diverse array" of proteins (Gething (Exhibit 12) at page 41, left column last paragraph, lines 1-7) and to bind ATP, although it does not appear to hydrolyze ATP (Gething (Exhibit 12) at page 41, right column, last 2 sentences).

Therefore, in view of these results, which were observed with representative members of the hsp60, hsp70, and hsp90 families, it was apparent to those skilled in the art that distinct heat shock proteins nevertheless possessed highly conserved properties including the ability to bind adenine nucleotides and to bind peptides, even though substantial differences exist among these proteins with respect to their molecular weight, amino acid sequence, intracellular location and biochemical role in the cell.

(3) Utility of Hsp-peptide Complexes and Methods for Purification Thereof

Hsp70, hsp90, and gp96 isolated from tumor tissue were each capable of vaccinating animals against a subsequent challenge with that tumor (Udono (1994) "Comparison of Tumor-Specific Antigenicities of Stress-Induced Proteins gp96, hsp90, and hsp70," *J. Immunol.* 152: 5398-5403 ("Udono II") (Exhibit 16) at page 5398, Abstract, lines 1-7). In contrast to this data, hsp70 preparations isolated from tumor tissue using affinity chromatography on an ATP column were found to be non-immunogenic. The difference between the immunogenic and non-immunogenic preparations appeared to be the result of the presence of hsp70-bound peptides in the former, but not the latter preparation (Udono (1993) "Heat Shock Protein 70-Associated Peptides Elicit Specific Cancer Immunity," *J. Exp. Med.* 178: 1391-1396 ("Udono I") (Exhibit 15) at page 1391, right column, last 10 lines to page 1392, left column, first 4 lines; FIG. 3 at page 1393). The immunogenicity of these heat shock protein preparations was suggested to be due to immunogenic peptides associated with the heat shock proteins, rather than due to the hsp, *per se* (Udono II (Exhibit 16) at page 5401, right column, last paragraph).

In view of the above, those of ordinary skill in the art were aware that heat shock proteins were widely distributed in nature and carried out many cellular roles based upon their fundamental ability to bind to other proteins. Heat shock proteins were further characterized in that they formed non-covalent complexes with peptides and that they formed complexes with adenine nucleotides. It also appeared that hsp-peptide complexes isolated from tumor cells were

immunogenic. It was also clear to those of ordinary skill in the art that there was a need for the development of an improved method for purification of hsp-peptide complexes, which could be used for immunotherapy.

More specifically, it had been demonstrated in the art that complexes containing hsp70 (a member of the hsp70 family of heat shock proteins), as well as those complexes containing hsp90 and gp96 (members of the hsp90 family of heat shock proteins) that had been isolated from tumor tissue could be used to vaccinate animals against that tumor. Such complexes comprised hsp-bound peptides that were believed to be the basis of the immunogenicity of the heat shock protein complexes (Blachere (1993) "Heat Shock Protein Vaccines Against Cancer," *J. Immunotherapy* 14: 352-356 ("Blachere") (Exhibit 25) at page 352, Summary, lines 1-10; lines 1-5; Udono I (Exhibit 15) at page 1394, left column, first full paragraph and first sentence of the second full paragraph; Udono II (Exhibit 16) Abstract lines 1-7, and at page 5402, left column, first and second full paragraphs).

In view of the utility of hsp-peptide complexes comprising heat shock proteins from different families (*e.g.* both the hsp70 and the hsp90 families), it would have been desirable to purify hsp-peptide complexes comprising hsp70 as well other hsp-peptide complexes comprising a heat shock protein other than hsp70 since the art had indicated that both "groups" (*i.e.* hsp70-containing complexes and hsp complexes comprising an hsp other than hsp70, *e.g.* those comprising a member of the hsp90 family, such as hsp90 and gp96) appeared to be therapeutically useful.

Accordingly, positive results developed using either "group" of complexes would motivate those of ordinary skill in the art to substitute heat shock proteins of the alternate group in the recited methods and complexes in light of the therapeutic utility of such complexes. Moreover, those of ordinary skill in the art would have done so with a reasonable expectation of success since the claimed methods and complexes exploit highly conserved properties of heat shock proteins (peptide binding and adenine ribonucleotide binding) rather than other, physical properties, such as molecular weight and amino acid sequence, that distinguish individual hsp species.

(4) Specific Traits and Properties of Individual Heat Shock Proteins That Are Conserved Across Family "Boundaries": Non-hsp70 (*e.g.* hsp90 family members) and hsp70 Family Members

Many heat shock protein species have been identified in the art (*e.g.* protein chaperones include members of the hsp70, and hsp90 families (Gething (Exhibit 12) at page 35, left column, last paragraph, through line 6, first paragraph, right column, and Tables 1 and 2 at pages 35 and 37, respectively). Despite the reported differences, *e.g.* molecular weight, seen between members of different hsp families, they share two specific traits that are highly conserved among heat shock proteins even when considered as a "superfamily" encompassing, *e.g.* the hsp70 and hsp90 protein families: (1) adenine ribonucleotide binding and (2) peptide binding. As demonstrated above and as shown in the sections to follow, at the time of the present invention, those skilled in the art appreciated that both hsp70 as well as non-hsp70 heat shock proteins possessed these two highly conserved properties, even though substantial differences existed among hsps with respect to their molecular weight, amino acid sequence, intracellular location and specific intracellular role.

(a) Known Properties of Hsp90 Family Members gp96 and grp94

Before September 20, 1996, the filing date of the application to which the '608 patent ultimately claims priority, gp96 and grp94 were considered to be the same protein by those of ordinary skill in the art (Nieland (1996) *Proc. Natl. Acad. Sci.* 93: 6135-6139 ("Nieland") (Exhibit 24) at page 6135, left column, first sentence: "gp96, also known as GRP94, is a member of the HSP90 family..."; and Li (Exhibit 14) at page 3143, right column, first sentence of first full paragraph: "Comparison of the gp96 sequence to known sequences revealed significant homology with the heat shock protein (HSP) hsp90 and possible identity with the glucose-related protein grp94." (Citations omitted); *also see* Exhibit 23 (amino acid sequence comparison between gp96 and grp94; *also see* fn. 8, below). Accordingly, Fordham submits that the following information applies to grp94 as well as to gp96.

As indicated above, it had been established in the prior art that gp96 possessed an ATP-binding site, that gp96 bound ATP, that gp96 formed stable binary complexes with peptides (gp96-peptide) and that gp96 formed stable binary complexes with ADP (gp96-ADP) (Li

(Exhibit 14) at page 3143, Abstract; page 3144, left column, first full paragraph, first sentence; page 3144, left column, third full paragraph; page 3145 Fig. 3B; and at page 3147, paragraph entitled "Gp96 is associated with peptides"). It was also known that gp96-peptide complexes could be useful for the prevention and treatment of cancer and infectious disease, apparently as a result of the presence of immunogenic peptides non-covalently bound to gp96 (Li (Exhibit 14) at page 3143, Abstract).

(b) Known Properties of the Hsp90 Family Member hsp90

It was also known in the art that hsp90 and gp96 were members of the same heat shock protein family, that hsp90 was considered the cytosolic counterpart of gp96 (Udono I (Exhibit 15) at page 1391, left column, first paragraph, last sentence) and that hsp90 and gp96 shared substantial amino acid sequence homology (46% identity and 64% similarity, *see* Exhibit 23).

Moreover, it was also known that hsp90 bound ATP (Li (Exhibit 14) at page 3144, left column, first full paragraph, and Fig. 2, right column), and that hsp90 could be bound to and eluted from an ATP-column (Csermely (1991) *J. Biol. Chem.* 266(8): 4943-4950 ("Csermely") (Exhibit 26), at page 4945, right column, Table 1), and that the ATP-binding site of hsp90 was closely related to that of gp96. [8]

Hsp90 had also been reported to bind to peptides and to a "diverse array" of proteins (Gething (Exhibit 12), at page 41, left column, last paragraph, lines 1-7); Udono II (Exhibit 16) at page 5402, left column, last paragraph). It was also known that hsp90-peptide complexes could be useful for the prevention and treatment of cancer and infectious disease, apparently as a result of the presence of immunogenic peptides non-covalently bound to hsp90 (Blachere (Exhibit 25) at page 352, Abstract).

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[8] The ATP binding-region of gp96 has been identified within a 25 amino acid sequence (amino acids 154 to 178 of GenBank Accession No. gi: 18579009) beginning with the amino acids GNTLGRGT and ending with the amino acids KEEASDYLELD, where the 7 underlined residues are highly conserved (Li (Exhibit 14) at page 3144, Fig. 1). The corresponding 25 amino acid sequence in hsp90 has 12 amino acids that are identical (48% identity) to those in gp96 as well as 5 amino acids that "positively" correspond to those in gp96 (*i.e.* conservative replacements, such as serine for threonine, or aspartic acid for glutamic acid) (for a total of 17 residues either identical or positive, *i.e.* 68%). Of the 7 highly conserved residues in the gp96 sequence above, 6 are identical in the hsp90 sequence (Exhibit 23; amino acid sequence comparison between gi: 18579009 (gp96) and gi: 32488 (hsp90)).

(c) Known Properties of the Hsp70 Family Member hsp70

It had been established in the prior art that hsp70 bound ATP, formed stable binary complexes with peptides (hsp70-peptide), formed stable binary complexes with ADP (hsp70-ADP), and that hsp70-peptide complexes could be useful for the prevention and treatment of cancer and infectious disease, apparently as a result of the presence of immunogenic peptides non-covalently bound to hsp70 (Li (Exhibit 14) at page 3144, left column, third full paragraph, and page 3145, Fig. 3B; Udono I (Exhibit 15) at page 1391, Abstract, and Fig. 4, at page 1395; Udono II (Exhibit 16) at page 5402, left column, last paragraph; and Blachere (Exhibit 25) at page 352, Abstract).

B. The Claimed Methods and Complexes of UNM's '608 Patent

The method of claim 1, the method of claim 2, and the complexes of claim 3 of UNM's '608 patent reflect the ability of each heat shock protein to form a stable ternary complex with a peptide and an ADP ligand. For the reasons provided herein, the methods of claims 1 and 2, as well as the complexes of claim 3 of UNM's '608 patent, drawn to "non-hsp70" complexes, would have been obvious to one of ordinary skill in the art in view of the same methods and complexes involving hsp70 in independent claims 62, 65, and 68 of Fordham's above-captioned application.

This expectation would have been based on the fact that the claimed methods and complexes rely upon shared properties of heat shock proteins, *i.e.* the ability to bind peptides and to bind adenine ribonucleotides, and to be independent of *e.g.* the molecular weight and amino acid sequence differences that exist between the various heat shock proteins encompassed within the recited non-hsp70 subgenus.

That is, although the vast collection of heat shock proteins encompassed within the subgenus recited in each of the claims of the '608 patent includes distinct molecules as compared to hsp70, all of these proteins, by definition, are recognized members of the heat shock protein "superfamily." As such, they share common, highly conserved properties with hsp70. The shared properties include the ability to bind peptides and the ability to bind adenine

ribonucleotides, *i.e.* the particular traits underlying each of the claims of UNM's '608 patent. Therefore, in light of the successful demonstration of a species falling within the scope of claim 1or 2 of the '608 patent or within the scope of Fordham claim 62 or 65, those of ordinary skill in the art, at the time of the invention, would have recognized that other hsp complexes could be purified or could be synthesized according to the demonstrated method. Similarly, it would have been apparent that other stable hsp-ADP-peptide complexes could also exist in light of the demonstration of a complex falling within the scope of claim 3 of UNM's '608 patent or within the scope of Fordham claim 68.

Moreover, those of ordinary skill in the art would have recognized that these demonstrated phenomena would be independent of the molecular weight, amino acid sequence, and structure of the particular hsp used for the demonstration. For example, affinity chromatography, such as the purification method of claim 1 of the '608 patent, "is the only commonly available technique that is based on the biological *rather than physical properties* of proteins." (Lillehoj (1989) "Protein Purification," in *Advances in Biochemical Engineering/Biotechnology* Ed. A. Fiechter, Springer-Verlag, Berlin, Heidelberg, pages 20-71 ("Lillehoj") (Exhibit 17) at page 22, last 2 lines to page 23 first line, emphasis added). Therefore, it was well known in the art that affinity chromatography is based upon the affinity of a protein for an immobilized ligand and does not depend upon other properties, such as the molecular weight, amino acid sequence, or structure of that protein.

Therefore, upon a demonstration of the existence of a first hsp-ADP-peptide complex, or of the claimed methods for purification or synthesis of such complexes, and in view of the common traits of hsps described above, it would have been apparent to those of ordinary skill in the art at the time of the invention, that other heat shock proteins could be substituted for the heat shock protein involved in the demonstrated complex or method.

Motivation for making such a substitution was provided by the expectation that such complexes might be useful for the prevention and treatment of cancer and infectious disease, and by the knowledge that prior-art methods were either inefficient or did not provide the desired immunogenic, peptide-containing hsp complexes (Udono I (Exhibit) 15, at page 1392, right column, second full paragraph through page 1393, left column, first paragraph).

C. Findings and Decisions of Interference 104,761

Interference 104,761 determined that independent, generic claims 1 and 13 of UNM's parent '332 patent, which, respectively, recite a method for the purification and a method for the synthesis of hsp complexes, were directed toward the same patentable invention as claims 62 and 65 of Fordham that recited methods for the purification and synthesis of hsp70 complexes. More specifically, the Board found that the recited methods for the purification and synthesis of non-hsp70 complexes were obvious over the same methods for the isolation and purification of hsp70 complexes (Exhibit 18: Interference 104,761, Paper 98 "Decision on Motions," at page 43, first paragraph, last sentence). In this context, Fordham notes that claims 1 and 2 of UNM's '608 patent are essentially identical to claims 1 and 13 of UNM's '332 patent, except for the negative proviso ("wherein said heat shock protein complexes are non-hsp70 heat shock protein complexes") that is recited in the claims of the '608 patent.

In addition, UNM's dependent claims 3-5, 7-12, 15-17, and 19-23 of the '332 patent were defined as or designated as corresponding to counts 1 and 2 of Interference 104,761, which recited methods for the purification and the synthesis, respectively, of heat shock protein 70 complexes. UNM's dependent claims 3-5, 7-12, 15-17, and 19-23 of the '332 patent recited, collectively, purification and synthesis methods for heat shock protein complexes in which the hsp was selected from among: members of the hsp70 family (including *inter alia* the recited species DnaK, Ssa, Ssb, Ssc, grp75, and Bip(Grp78)), from among members of the hsp60 family (including the recited species hsp60, hsp65, rubisco binding protein, TCP-1, GroEL/ES, Mif4, TCPalpha and TCPbeta), from among members of the alleged "hsp104-105 family" (including the recited species hsp104, hsp105, and hsp110), and from among members of the hsp90 family (including the recited species hsp 90, gp96, and grp94). Fordham notes that all of these recited heat shock protein species fall within the scope of the genus of non-hsp70 heat shock proteins recited in claims 1 and 2 of UNM's '608 patent.

The methods recited in claims 1 and 2 of UNM's '608 patent for non-hsp70 complexes are not patentably distinct over the same methods for hsp70 complexes. This issue was, in fact, specifically raised in UNM's Preliminary Motion 1, filed in Interference 104,761. In this motion, UNM requested that certain claims reciting the purification and the synthesis of

non-hsp70 complexes (including hsp60, hsp65, rubisco binding protein, TCP-1, GroEL/GroES, Mif4, TCPalpha, TCPbeta, hsp104, hsp105, hsp110, hsp90, gp96, and grp94) be designated as not corresponding to the counts. The Board denied this motion.

In its Decision on this Motion, the Board noted that the art had demonstrated adenine ribonucleotide binding and protein binding were common properties identified in certain heat shock proteins (Exhibit 18, page 42, last paragraph). In fact, the Board concluded that

> a person having ordinary skill in the art at the time UNM filed its applications would have considered isolation of hsp-protein complexes using an ADP-matrix to have been obvious for any heat-shock protein with an ATP-binding domain and a protein-binding domain in view of Fordham's claimed hsp70 invention. (Exhibit 18, page 43, first paragraph, last sentence).

These findings were deemed to be "consistent with UNM's view," since, according to the Board, UNM's specification had provided essentially no enabling details regarding any hsp other than hsp70. That is, according to the Board, UNM was confident that those skilled in the art would be able to carry out the claimed methods involving non-hsp70 complexes in view of its disclosure of methods for the purification and synthesis of hsp70 complexes (Exhibit 18; Decision on Motions, Interference 104,761, Paper 98, at page 43, first paragraph). According to the Board, "UNM apparently viewed the listed heat-shock proteins as an interchangeable class" for use in the claimed methods for purification and synthesis of hsp complexes (*Id.*).

In view of the above it is apparent that, in its specification (common to UNM's '332, '716, '141, and '608 patents), UNM has relied solely on the mere listing of hsp species for written description support and enablement of UNM's claimed methods for purification and for synthesis of non-hsp70 complexes as well as for the claimed non-hsp70-containing complexes *per se*. That is, as noted above, UNM has necessarily relied upon an implicit teaching that heat shock proteins are such highly conserved molecules having common biological activities that disclosure of a method relating to hsp70 or a complex involving hsp70 makes obvious the use of the same method and existence of ternary hsp-ADP-peptide complexes for all hsp species listed.

Accordingly, Interference 104,761, further established that the ternary hsp-ADP-peptide complexes recited in UNM's parent '716 patent that involved hsp-peptide complexes in which the hsp was selected from the hsp70 family of heat shock proteins (including

the recited species DnaK, Ssa, Ssb, Ssc, grp75, Bip(Grp78), which fall within the genus of non-hsp70 proteins recited in claim 3 of UNM's '608 patent) were also directed toward the same patentable invention as the corresponding claims of Fordham that recited hsp70 complexes. Moreover, in response to Fordham Miscellaneous Motion 4, the Board redeclared Interference 104,761 and further designated claims 1-18 of UNM's '141 patent as corresponding to count 3. Specifically, the Board found that claims to ternary hsp90, gp96, and grp94 complexes (which also fall within the scope of claim 3 of UNM's '608 patent) define the same patentable invention as claims reciting the corresponding hsp70 complexes (Exhibit 19; Notice Redeclaring Interference, paper 107, Interference 104,761).

D. Claim 1 of UNM's '608 Patent and Fordham Claim 62 Define the Same Patentable Invention and, Therefore, Are Directed Toward Interfering Subject Matter

Fordham submits that claim 1 of UNM's '608 patent and claim 62 of Fordham's above-identified application define interfering subject matter since each would either anticipate the other or render the other obvious if it were prior art, as demonstrated below (37 C.F.R. § 41.203(a)).

Claim 1 of UNM's '608 patent recites:

> A method for purifying heat shock protein complexes comprising the steps of:
>
> adding a solution containing heat shock protein complex associated with at least one member of the group consisting of peptides, polypeptides, denatured proteins and antigens to an ADP matrix column containing an ADP matrix to bind the heat shock proteins complexes to the ADP matrix; and
>
> adding a buffer containing ADP to the column to remove the heat shock protein complexes in an elution product, wherein said heat shock protein complexes are non-hsp70 heat shock protein complexes.

Claim 1 of UNM's '608 patent recites a genus of heat shock proteins that encompasses all heat shock proteins, other than the heat shock protein species, hsp70 (*see* Section I (B)(2), above). Accordingly, claim 1 of UNM's '608 patent reads on all members of the hsp 70 family other than the particular species, hsp70.

Claim 62 of Fordham's '754 application recites:

> A method for purifying heat shock protein 70 complexes comprising the steps of:
>
> adding a solution containing a heat shock protein 70 complex comprising a heat shock protein 70 associated with at least one member of the group consisting of peptides and proteins, to an ADP matrix column containing an ADP matrix to bind the heat shock protein 70 complexes to the ADP matrix; and
>
> adding a buffer containing ADP to the column to remove the heat shock protein 70 complexes in an elution product.

The phrase "hsp70" in Fordham claim 62 refers to the hsp70 family of heat shock proteins. This is demonstrated, for example, by Fordham's dependent claim 64, which recites the method of Fordham claim 62 in which the heat shock protein 70 complexes comprise complexes in which the heat shock protein 70 comprises one of the group consisting of DnaK proteins from prokaryotes; Ssa, Ssb, and Ssc from yeast; and hsp70, grp75 and Bip(Grp78) from eukaryotes. Therefore, in light of the doctrine of claim differentiation, it is clear that Fordham claim 62 is a generic claim that is directed toward a method for purifying heat shock protein complexes, in which the hsp is a member of the hsp70 family of heat shock proteins, *i.e.* the claimed method is not limited to the species hsp70.

(1) Assuming Claim 1 of the '608 Patent is Prior Art

For the purposes of the first part of the two-way patentability analysis to establish the existence of an interference-in-fact, the prior art would be deemed to include claim 1 of UNM's '608 patent as well as the information provided in Sections II (A-C) above. In the present context, the prior art would include a method for purifying hsp complexes that was known to be useful for every heat shock protein other than hsp70, as well as the knowledge that hsp70 formed a stable complex with a peptide and that hsp70 formed a stable complex with ADP.

In addition, if the method of claim 1 of the '608 patent were in the prior art, it would establish that heat shock proteins in general, including members of the hsp70 family other than the species hsp70 (*i.e.*, for example, a DnaK proteins from a prokaryote; Ssa, Ssb, and Ssc

from yeast; and grp75 and Bip(Grp78) from a eukaryote), could bind to a peptide and to matrix-bound ADP simultaneously and that such hsp complexes could be eluted with ADP. In this instance, Fordham claim 62 would be anticipated since it is directed toward a method of purification of hsp70 complexes in which the hsp70 is a member of the hsp70 family and the art would have disclosed a method for the purification of complexes comprising an hsp that is a member of the hsp70 family.

Again, the method of claim 1 of the '608 patent would establish that heat shock proteins in general, and *e.g.* gp96 in particular, could bind to a peptide and to matrix-bound ADP simultaneously and that such hsp complexes could be eluted with ADP. Accordingly, in view of this teaching, the question would be whether or not one of ordinary skill in the art would be motivated to substitute hsp70 in the claimed method, and, in doing so, would that skilled person have a reasonable expectation of success.

Motivation to use the method of claim 1 of the '608 patent for the purification of hsp70-containing complexes would be provided by the knowledge in the art (1) that such complexes might be useful for the treatment and prevention of infectious disease and cancer and (2) that alternative purification methods were relatively inefficient or apparently did not yield the desired immunogenic, peptide-containing complexes (Udono I (Exhibit) 15, at page 1392, right column, third full paragraph through page 1393, left column, first paragraph).

One of ordinary skill in the art would have had a reasonable expectation of success, in this context, of using this purification method for hsp70-containing complexes in view of the prior art's disclosure of: (1) the ability of heat shock proteins to bind ADP and a peptide simultaneously, (2) the conservation of adenine nucleotide-binding and peptide-binding activities among heat shock proteins, (3) the ability of hsp70 (like *e.g.* gp96) to form stable binary complexes with ADP, and (4) the ability of hsp70 (like *e.g.* gp96) to form stable binary complexes with peptides.

Therefore, each element of claim 62 of Fordham's above-captioned application would have been disclosed in the prior art. Moreover, the art would have motivated one of ordinary skill in the art to substitute hsp70-complexes for another non-hsp70 heat shock protein complex, *e.g.* a gp96 complex, in the method of claim 1 of UNM's '608 patent, with the expectation that the claimed method could be used successfully for isolation of those complexes.

Accordingly, Fordham submits that claim 62 of the above-application would have been obvious over claim 1 of UNM's '608 patent, in view of the art.

(2) Assuming Fordham Claim 62 is Prior Art

For the purposes of the second part of the two-way patentability analysis to establish the existence of an interference-in-fact, the prior art includes the information in Sections II (A-C) above, as well as Fordham claim 62 and those claims dependent thereon. Fordham's claims disclose the purification of hsp-peptide complexes on an ADP-matrix, where the hsp is a member of the hsp70 family, including, but not limited to the species hsp70, DnaK, Ssa, Ssb, Ssc grp75, and Bip(Grp78) (as specifically recited in Fordham allowed claim 64 of the above-captioned application).

Claim 1 of UNM's '608 patent and claim 62 of Fordham differ in that the former is directed toward the purification of any hsp complex that does not include the species, hsp70, while the latter recites the purification of complexes in which the hsp is a member of the hsp70 family. As such, it is apparent that claim 1 of UNM's '608 patent would be anticipated by the prior art which discloses purification of hsp complexes (*e.g.* those comprising DnaK, Ssa, Ssb, Ssc, grp75, and Bip(Grp78)) that fall within the scope of the recited subgenus.

Even if Claim 1 of UNM's '608 patent were deemed not to be anticipated by claim 62 of Fordham, it would be obvious over that claim of Fordham in view of the art. In this context, motivation to substitute a non-hsp70 hsp for hsp70 in the purification method of Fordham claim 62 would be provided by the knowledge that non-hsp70 complexes (*e.g.* those including hsp90 and gp96) might be useful for the treatment and prevention of infectious disease and cancer.

One of ordinary skill in the art would have had a reasonable expectation of success in using this purification method for non-hsp70-containing complexes in view of the prior art's disclosure of the ability hsp70 to bind ADP and a peptide simultaneously, the conservation of adenine nucleotide-binding and peptide-binding activities among heat shock proteins, the ability of non-hsp70 proteins (*e.g.* gp96) like hsp70, to form stable binary complexes with ADP, and the ability of non-hsp70 proteins (*e.g.* gp96) like hsp70, to form stable binary complexes with peptides.

Consequently, each element of claim 1 of UNM's '608 patent would have been disclosed in the prior art. Moreover, the art would have motivated one of ordinary skill in the art to substitute non-hsp70 complexes (*e.g.* hsp90 and gp96 complexes), for hsp70 complexes in the method of claim 62 of Fordham's above-captioned application. Accordingly, Fordham submits that claim 1 of the UNM's '608 patent would have been obvious over claim 62 of Fordham's above-captioned application in view of the art.

Therefore, in view of the above, claim 1 of UNM's '608 patent and claim 62 of Fordham's above-captioned application would each be anticipated by or be obvious over the other, where the other is deemed to be in the prior art. Accordingly, claim 1 of UNM's '608 patent and claim 62 of Fordham's above-captioned application define interfering subject matter and are directed toward same patentable invention. Therefore, an interference-in-fact exists between these two claims.

E. Claim 2 of UNM's '608 Patent and Fordham Claim 65 Define the Same Patentable Invention

Fordham submits that claim 2 of UNM's '608 patent and claim 65 of Fordham's above-identified application define interfering subject matter since each would either anticipate the other or render the other obvious if it were prior art, as demonstrated below (37 C.F.R. § 41.203(a)).

Claim 2 of UNM's '608 patent recites:

> A method for synthesizing heat shock protein complexes comprising the steps of:
>
> adding a solution containing a heat shock protein to an ADP matrix column containing an ADP matrix to bind the heat shock protein to the ADP matrix; adding a complexing solution comprising a complexing agent selected from the group consisting of peptides, polypeptides, denatured proteins and antigens to the column, to form heat shock protein complexes with the heat shock protein with the heat shock protein bound to the ADP matrix column; and
>
> adding a buffer containing ADP to the column to remove the heat shock protein complexes in an elution product, wherein said heat shock protein complexes are non-hsp70 heat shock protein complexes.

Claim 2 of UNM's '608 patent recites a genus of heat shock proteins that encompasses all heat shock proteins other than the heat shock protein species, hsp70 (*see* Section I(B)(2) above). Accordingly, claim 2 of UNM's '608 patent reads on all members of the hsp 70 family other than the particular species, hsp70.

Claim 65 of Fordham's '754 application recites:

> A method for synthesizing heat shock protein 70 complexes, comprising adding a heat shock protein 70 and an antigenic molecule selected from the group consisting of peptides and proteins, to a buffer containing ADP to allow the heat shock protein 70 to bind to the antigenic molecule and ADP to form a heat shock protein 70 complex.

The phrase "hsp70" in Fordham claim 65 refers to the hsp70 family of heat shock proteins. This is demonstrated, for example, by Fordham dependent claim 67, which recites that the method of claim 65 in which the heat shock protein 70 comprises one of the group consisting of DnaK proteins from prokaryotes; Ssa, Ssb, and Ssc from yeast; hsp70, grp75 and Bip(Grp78) from eukaryotes. Accordingly, in light of the doctrine of claim differentiation, it is clear that Fordham claim 65 is directed toward a method for the synthesis of heat shock protein complexes in which the hsp is a member of the heat shock protein 70 family; *i.e.* Fordham claim 65 is not limited to the species hsp70.

(1) Assuming Claim 2 of the '608 Patent is Prior Art

For the purposes of the first part of the two-way patentability analysis to establish the existence of an interference-in-fact, the prior art would be deemed to include claim 2 of UNM's '608 patent as well as the information provided in Sections II (A-C) above. The prior art would, therefore, include not only a method for synthesizing hsp complexes useful for every known hsp other than hsp70, but also the knowledge that hsp70 was known to form a stable complex with a peptide and that hsp70 was known to form a stable complex with ADP.

In addition, if the method of claim 2 of the '608 patent were in the prior art, it would establish that heat shock proteins in general, including members of the hsp70 family other than the species hsp70 (*i.e.*, for example, DnaK protein from a prokaryote; Ssa, Ssb, and Ssc

from yeast; and grp75 and Bip(Grp78) from a eukaryote), could bind to a peptide and ADP simultaneously to form hsp complexes. In this instance, Fordham claim 65 would be anticipated since it is directed toward a method of synthesis of hsp70 complexes in which the hsp70 is a member of the hsp70 family and the art would have disclosed a method for the synthesis of hsp complexes falling within the scope of Fordham claim 65.

Again, the method of claim 2 of the '608 patent would establish that non-hsp70 heat shock proteins, in general, and *e.g.* gp96 in particular, could bind to a peptide and to ADP simultaneously. Accordingly, in view of this teaching, the question would be whether or not one of ordinary skill in the art would be motivated to substitute hsp70 in the claimed method, and, in doing so, would that skilled person have a reasonable expectation of success.

Motivation to use the method of claim 2 of the '608 patent for the synthesis of hsp70-containing complexes would be provided by the knowledge in the art that such complexes might be useful for the treatment and prevention of infectious disease and cancer.

One of ordinary skill in the art would have had a reasonable expectation of success in using this synthesis method for hsp70-containing complexes in view of the prior art's disclosure of the ability of non-hsp70 heat shock proteins to bind ADP and a peptide simultaneously, the conservation of adenine nucleotide-binding and peptide-binding activities among heat shock proteins, the ability of hsp70 (like non-hsp70 heat shock proteins such as gp96) to form stable binary complexes with ADP, and the ability of hsp70 (like non-hsp70 heat shock proteins such as gp96 or hsp90) to form stable binary complexes with peptides.

Therefore, each element of claim 65 of Fordham's above-captioned application would have been disclosed in the prior art. Moreover, the art would have motivated one of ordinary skill in the art to substitute hsp70 for a non-hsp70 heat shock protein, *e.g.* gp96 or hsp90, in the method of claim 2 of UNM's '608 patent, with the expectation that the claimed method could be used successfully for synthesis of those complexes. Accordingly, Fordham submits that claim 65 of Fordham's above-captioned application would have been obvious over claim 2 of UNM's '608 patent, in view of the art.

(2) Assuming Fordham Claim 65 is Prior Art

For the purposes of the second part of the two-way patentability analysis to establish the existence of an interference-in-fact, the prior art includes the information in Sections (A-C) above, as well as Fordham claim 65 and those claims dependent thereon. Fordham's claims disclose the synthesis of hsp-peptide complexes, where the hsp is a member of the hsp70 family, including, but not limited to the species hsp70, DnaK, Ssa, Ssb, Ssc, grp75, and Bip(Grp78) (as specifically recited in allowed claim 67 of the above-captioned application).

Claim 2 of UNM's '608 patent and claim 65 of Fordham differ in that the former is directed toward the synthesis of any hsp complex that does not include the species hsp70, while the latter recites the synthesis of complexes in which the hsp is a member of the hsp70 family. As such, it is apparent that claim 2 of UNM's '608 patent would be anticipated by prior art that discloses synthesis of hsp complexes (*e.g.* those complexes comprising DnaK, Ssa, Ssb, Ssc grp75, and Bip(Grp78)) that fall within the scope of the recited subgenus of claim 2 of UNM's '608 patent.

Even if Claim 2 of UNM's '608 patent were deemed not to be anticipated by claim 65 of Fordham, it would be obvious over that claim of Fordham in view of the art. Motivation to substitute a non-hsp70 heat shock protein for hsp70 in the synthesis method of Fordham claim 65 would be provided by the knowledge that non-hsp70 complexes (*e.g.* those including hsp90 and gp96) might be useful for the treatment and prevention of infectious disease and cancer.

One of ordinary skill in the art would have had a reasonable expectation of success in using this synthesis method for non-hsp70-containing complexes (such as hsp90 and gp96), in view of the prior art's disclosure of the ability of hsp70 to bind ADP and a peptide simultaneously, the conservation of adenine nucleotide-binding and peptide-binding activities among heat shock proteins, the ability of non-hsp70 heat shock proteins (such as gp96 or hsp90), like hsp70, to form stable binary complexes with ADP, and the ability of non-hsp70 heat shock proteins (such as gp96), like hsp70 to form stable binary complexes with peptides.

Therefore, each element of claim 2 of UNM's '608 patent would have been disclosed in the prior art. Moreover, the art would have motivated one of ordinary skill in the art to substitute non-hsp70 complexes (*e.g.* hsp90 and gp96 complexes), for hsp70 complexes in the method of claim 65 Fordham's above-captioned application. Accordingly, Fordham submits that claim 2 of UNM's '608 patent would have been obvious over claim 65 of Fordham's above-captioned application in view of the art.

Therefore, in view of the above, claim 2 of UNM's '608 patent and claim 65 of Fordham's above-captioned application would each be anticipated by or be obvious over the other, where the other is deemed to be in the prior art. Accordingly, claim 2 of UNM's '608 patent and claim 65 of Fordham's above-captioned application define interfering subject matter and are directed toward the same patentable invention. Therefore, an interference-in-fact exists between these two claims.

F. Claim 3 of UNM's '608 Patent and Fordham Claim 68 Define the Same Patentable Invention

Fordham submits that claim 3 of UNM's '608 patent and claim 68 of Fordham's above-identified application define interfering subject matter since each would either anticipate the other or render the other obvious if it were prior art, as demonstrated below (37 C.F.R. § 41.203(a)).

Claim 3 of UNM's '608 patent recites:

> An ADP-heat shock protein-peptide complex in purified form, wherein said heat shock protein complex is a non-hsp70 heat shock protein complex.

Claim 3 of UNM's '608 patent recites a genus of heat shock proteins that encompasses all heat shock proteins other than the heat shock protein species, hsp70. Accordingly, claim 3 of UNM's '608 patent reads on all members of the hsp 70 family other than the particular species, hsp70.

Claim 68 of Fordham's '754 application recites:

> An ADP-heat shock protein 70-peptide complex in substantially purified form as indicated by apparent homogeneity upon electrophoresis in a polyacrylamide gel.

The phrase "hsp70" in Fordham claim 68 refers to the hsp70 family of heat shock proteins. This is demonstrated, for example, by Fordham dependent claim 69 that recites the ADP-heat shock protein 70-peptide of claim 68, wherein said heat shock protein 70 comprises one of the group consisting of DnaK proteins from prokaryotes; Ssa, Ssb, and Ssc from yeast; hsp70, grp75 and Bip(Grp78) from eukaryotes. Accordingly, in light of the doctrine of claim differentiation, it is clear that Fordham claim 68 is generic and therefore it is not limited to the species hsp70.

(1) Assuming Claim 3 of the '608 Patent is Prior Art

For the purposes of the first part of the two-way patentability analysis to establish the existence of an interference-in-fact, the prior art would be deemed to include claim 3 of UNM's '608 patent as well as the information provided in Sections II (A-C) above. That is, the prior art would include the knowledge that hsp 70 was able to form a stable complex with a peptide and that hsp70 was able to form a stable complex with ADP.

In addition, if the complexes of claim 3 of the '608 patent were in the prior art, it would establish that heat shock proteins in general, including members of the hsp70 family other than the species hsp70 (*i.e.*, for example, DnaK proteins from prokaryotes; Ssa, Ssb, and Ssc from yeast; and grp75 and Bip(Grp78) from eukaryotes), could bind to a peptide and ADP simultaneously to form the claimed complexes. In this instance, Fordham claim 68 would be anticipated since it is directed toward hsp70 complexes in which the hsp70 is a member of the hsp70 family and the art would have disclosed hsp complexes comprising hsp70 family member that would, therefore, fall within the scope of Fordham claim 68.

Again, the complexes of claim 3 of UNM's '608 patent would establish that heat non-hsp70 heat shock proteins in general, and *e.g.* gp96 in particular, could bind to a peptide and to ADP simultaneously to form a stable ternary complex. Accordingly, in view of this teaching, the question would be whether or not one of ordinary skill in the art would have been motivated to substitute hsp70 in the claimed complex, and, in doing so, would that skilled person have a reasonable expectation of success.

Motivation to substitute hsp70 for another hsp in the ternary hsp-ADP-peptide complexes of claim 3 of UNM's '608 patent would be provided by the knowledge in the art that

such complexes might be useful for the treatment and prevention of infectious disease and cancer.

One of ordinary skill in the art would have expected that stable ternary hsp70-ADP-peptide complexes existed in view of the existence of (1) knowledge that stable complexes involving every hsp other than hsp70, *e.g.* including gp96-ADP-peptide complexes existed; (2) in view of the prior art's disclosure of the ability of heat shock proteins to bind ADP and a peptide simultaneously, (3) the conservation of adenine nucleotide-binding and peptide-binding activities among heat shock proteins, (4) the ability of hsp70 (like other non-hsp70 heat shock proteins such as hsp 90 or gp96) to form stable binary complexes with ADP, and (5) the ability of hsp70 (like other non-hsp70 heat shock proteins such as hsp 90 or gp96) to form stable binary complexes with peptides.

Therefore, each element of claim 68 of Fordham's above-captioned application would have been disclosed in the prior art. Moreover, the art would have motivated one of ordinary skill in the art to substitute hsp 70 for the non-hsp70 heat shock protein (such as hsp90 or gp96) of the complexes of claim 3 of UNM's '608 patent, with a reasonable expectation of success. Accordingly, Fordham submits that claim 68 of the above-captioned application would have been obvious over claim 3 of UNM's '608 patent, in view of the art.

(2) Assuming Fordham Claim 68 is Prior Art

For the purposes of the second part of the two-way patentability analysis to establish the existence of an interference-in-fact, the prior art includes the information in the Section II (A-C), above, as well as Fordham's claim 68 and those claims dependent thereon. Fordham's claims, therefore, disclose hsp-ADP-peptide ternary complexes in which the heat shock protein is a member of the hsp70 family of proteins, which includes, *inter alia*, the protein species, hsp70. Accordingly, the only difference between independent claim 3 of UNM's '608 patent and the prior art, is that the hsp recited as part of the ternary hsp-ADP-peptide complexes of claim 3 is any hsp, *e.g.* DnaK, Ssa, Ssb, Ssc, Grp75, Grp78(BiP), hsp90, gp96, and grp94, rather than hsp70.

With respect to the question as to whether, in view of the above, it would have been obvious to one of ordinary skill in the art to substitute a non-hsp70 heat shock protein (*e.g.*

hsp90, gp96, or grp94) for hsp70 in the ternary hsp70-ADP-peptide complexes recited in Fordham's involved claims to arrive at the invention defined by claim 3 of UNM's '608 patent, Fordham submits the following.

One of ordinary skill in the art would have been motivated to substitute a non-hsp70 heat shock protein (*e.g.* gp96 or hsp90) for the hsp70 in the ternary complexes of Fordham claim 68, with the knowledge that such complexes might be useful for the prevention and treatment of cancer and infectious disease (Blachere (Exhibit 25) at page 352, Abstract).

Moreover, one of ordinary skill would have had a reasonable expectation of success in forming ternary non-hsp70-ADP-peptide complexes (*e.g.* hsp90-ADP-peptide or gp96-ADP-peptide complexes) in view of the prior art's disclosure of hsp70-ADP-peptide complexes and in light of: (1) the adenine nucleotide binding and peptide sequence binding activities conserved among heat shock proteins; (2) the ability of non-hsp70 heat shock proteins (such as gp96) like hsp70, to form stable binary complexes with ADP; and (3) the ability of non-hsp70 heat shock proteins (such as gp96) like hsp70, to form stable binary complexes with peptides.

Therefore, each element of the invention of claim 3 of UNM's '608 patent had been disclosed in the prior art. Moreover, the prior art also provided motivation to one of ordinary skill in the art to substitute a non-hsp70 heat shock protein (*e.g.* gp96) for hsp70 in the ternary complex recited in Fordham claim 68, for example, with a reasonable expectation of success. Accordingly, Fordham submits that claim 3 of UNM's '608 patent would have been obvious over Fordham claim 68.

Therefore, in view of the above, claim 3 of UNM's '608 patent and claim 68 of Fordham's above-captioned application would each be anticipated by or be obvious over the other, where the other is deemed to be in the prior art. Accordingly, claim 3 of UNM's '608 patent and claim 68 of Fordham's above-captioned application are directed toward interfering subject matter and are directed toward the same patentable invention. Therefore, an interference-in-fact exists between these two claims.

III. Fordham Proposed Counts 1, 2, and 3

Fordham Proposed Counts 1-3 are directed, respectively, toward a method for isolation of heat shock protein complexes, a method for the synthesis of heat shock protein complexes, and for ternary ADP-heat shock protein-peptide complexes *per se*. Fordham Proposed Counts 1 - 3 are analogous to Counts 1, 4(2), and 3, respectively, of Interference 104,761. The proposed counts include the interfering subject matter of the analogous counts of Interference 104,761, and are broad enough to insure that the best proofs of both parties will be included within the scope of each count but are narrow enough to avoid encompassing more than one separately patentable invention. (*see* **Appendix E** below, which compares Counts 1, 4(2), and 3 of Interference 104,761 with Fordham Proposed Counts 1, 2, and 3, respectively).

A. Fordham Proposed Count 1:

A method for purifying heat shock protein complexes comprising the steps of:

adding a heat shock protein complex comprising a heat shock protein associated with at least one member of the group consisting of peptides, polypeptides, denatured proteins and antigens to an ADP matrix column containing an ADP matrix to bind the heat shock protein complexes to the ADP matrix; and

adding a buffer containing ADP to the column to remove the heat shock protein complexes in an elution product;

wherein the heat shock protein is selected from the group consisting of hsp60, hsp65, rubisco binding protein, TCP-1, GroEL/GroES, Mif4, TCPalpha, TCPbeta, hsp104, hsp105, hsp110, DnaK, Ssa, Ssb, Ssc, hsp70, Grp75, Grp78(BiP), hsp90, gp96, and grp94.

OR

Claim 62 of Fordham's above-captioned '754 application (Alternative Count 1 of Interference 104,761):

A method for purifying heat shock protein 70 complexes comprising the steps of:

adding a solution containing a heat shock protein 70 complex comprising a heat shock protein 70 associated with at least one member of the group consisting of peptides and proteins, to an ADP matrix column containing an ADP matrix to bind the heat shock protein 70 complexes to the ADP matrix; and

adding a buffer containing ADP to the column to remove the heat shock protein 70 complexes in an elution product.

B. <u>Fordham Proposed Count 2</u>:

A method for synthesizing heat shock protein complexes comprising the steps of:

adding a solution containing a heat shock protein to an ADP matrix column containing an ADP matrix to bind the heat shock protein to the ADP matrix;

adding a complexing solution comprising a complexing agent selected from the group consisting of peptides, polypeptides, denatured proteins and antigens to the column to form a heat shock protein complex with the heat shock protein bound to the ADP matrix column; and

adding a buffer containing ADP to the column to remove the heat shock protein complex in an elution product;

wherein the heat shock protein is selected from the group consisting of hsp60, hsp65, rubisco binding protein, TCP-1, GroEL/GroES, Mif4, TCPalpha, TCPbeta, hsp104, hsp105, hsp110, DnaK, Ssa, Ssb, Ssc, hsp70, Grp75, Grp78(BiP), hsp90, gp96, and grp94.

OR

Claim 65 of Fordham's above-captioned application, as modified to recite the following (Alternative Count 4 of Interference 104,761):

A method of synthesizing heat shock protein 70 complexes, comprising contacting a heat shock protein 70 with an antigenic molecule selected from the

group consisting of peptides and proteins, and with a buffer containing ADP to allow the heat shock protein 70 to bind the antigenic molecule and to allow the heat shock protein 70 to bind to the ADP to form a heat shock protein 70 complex.

C. **Fordham Proposed Count 3:**

An ADP-heat shock protein-peptide complex in purified form, wherein the heat shock protein is selected from the group consisting of DnaK, Ssa, Ssb, Ssc, hsp70, Grp75, Grp78(BiP), hsp90, gp96, and grp94.

OR

Claim 68 of Fordham's above-captioned '754 application:

An ADP-heat shock protein 70-peptide complex in substantially purified form as indicated by apparent homogeneity upon electrophoresis in a polyacrylamide gel.

D. Fordham Proposed Counts 1-3 Are Proper

The prior Regulations provided that each count in an interference must define a separately patentable invention (37 C.F.R. § 1.601(f)), where the phrase "separately patentable invention" had been defined by the former 37 C.F.R. § 1.601(n) as follows:

> Invention "A" is a separate patentable invention with respect to invention "B" when invention "A" is new (35 U.S.C. 102) and non-obvious (35 U.S.C. 103) in view of invention "B" assuming invention "B" is prior art with respect to invention "A."

Moreover, the Patent and Trademark Office had determined that the "separately patentable" standard would not be applied on a mutual basis. To illustrate this point, the PTO had stated that two counts may appear in an interference where one count was directed toward a genus and the other count is directed toward a species that is patentable over that genus (49 FR 48416, 48434 (Dec. 12, 1984). Since a publication of the agency's Final Rule represents an interpretation of the Director's own regulations, it is controlling unless it is deemed to be "plainly erroneous or inconsistent with the regulation" (*see e.g. Eli Lilly & Co. v. Board of Regents of the University of Washington* 334 F.3d 1264, 1268, 67 USPQ2d 1161, 1164 (Fed. Cir.

2003)).

Currently, newly issued Board Rule 201 provides that "each count must define a patentably distinct invention." The standard for patentable distinctness is a one-way test; therefore, when comparing two counts, "[i]t is sufficient if the subject matter of either count, treated as prior art, would not have anticipated or rendered obvious the subject matter of the other count" (69 FR 155, at page 49991, left column, first paragraph).

It follows therefore, that two counts, directed toward inventions "A" and "B" respectively, may properly appear in an interference provided at least one of inventions "A" and "B" is new (35 U.S.C. 102) and non-obvious (35 U.S.C. 103) in view of the other.

Fordham's Proposed Counts 1-3 are analogous to the three counts in Interference 104,761. Since the Board, UNM, and Fordham never disputed the use of those counts in Interference 104,761, it can be inferred that the counts of Interference 104,761, and therefore Fordham Proposed Counts 1-3, are directed toward patentably distinct inventions.

Notwithstanding this conclusion, Fordham submits that Fordham Proposed Counts 1-3 are proper, for the reasons that follow. Fordham Proposed Counts 1 and 2 would not be anticipated by nor obvious over the ternary hsp-ADP-peptide complexes of Fordham Proposed Count 3. That is, Fordham submits that the existence of such complexes *per se* would not motivate those of ordinary skill to attempt to purify or synthesize those complexes according to the methods of Fordham Proposed Counts 1 or 2, respectively. Moreover, even if, *arguendo*, there were any such motivation, Fordham submits that the existence of the complexes *per se* would not provide those of ordinary skill in the art with a reasonable expectation of success that the desired complexes could be obtained using those methods. Accordingly, Fordham Proposed Count 3 defines a patentably distinct invention as compared to the inventions of Fordham Proposed Counts 1 and 2.

Similarly, the method of purification recited in Fordham Proposed Count 1 would not be obvious over the method of synthesis of Fordham Proposed Count 2. That is, even if there were any motivation to modify the methods of Fordham Proposed Count 2 in an attempt to arrive at the purification method of Count 1, one of ordinary skill in the art would not have a reasonable expectation of success. That is, those of ordinary skill would not have a basis for expecting that

hsp-peptide complexes would not only bind to an ADP-matrix with sufficient strength to allow extraneous proteins and peptides to be removed without displacing the hsp-peptide complexes, but would also be capable of being eluted with ADP, apparently without displacement of column-bound contaminants. Accordingly Fordham Proposed Counts 1 and 2 are directed toward patentably distinct inventions.

Consequently, each of Fordham's Proposed Counts 1-3 is directed toward a patentably distinct invention, and therefore, Fordham's Proposed Counts 1-3 are proper under Board Rule 201.

IV. Designation of Claims Corresponding to Fordham Proposed Counts 1-3

Under former 37 C.F.R. § 1.606, all claims in an application and an interfering patent which define the same patentable invention as a count shall be designated to correspond to the count. The former interference rules were clear with respect to what constituted "the same patentable invention," which was defined by former 37 C.F.R. § 1.601(n) as follows:

> Invention "A" is the same patentable invention as an invention "B" when invention "A" is the same as (35 U.S.C. 102) or is obvious (35 U.S.C. 103) in view of invention "B" assuming invention "B" is prior art with respect to invention "A". Invention "A" is a separate patentable invention with respect to invention "B" when invention "A" is new (35 U.S.C. 102) and non-obvious (35 U.S.C. 103) in view of invention "B" assuming invention "B" is prior art with respect to invention "A".

Accordingly, under former 37 C.F.R. § 1.606, the relevant inquiry involved a two-way determination as to whether or not a claim and the proposed count to which that claim would be designated would each be unpatentable, *i.e.* would be either novel or obvious in view of the art, when each, in turn, was deemed to be prior art to the other.

In contrast, current Board Rule 207(b)(2), provides that "[a] claim corresponds to a count if the subject matter of the count, treated as prior art to the claim, would have anticipated or rendered obvious the subject matter of the claim." Thus a claim will be designated as corresponding to a count "if the subject matter of the claim would have been anticipated by or obvious (alone or in combination with prior art) in view of the subject matter of the count" (69 FR 155, at page 49969, right column, first paragraph). Fordham also notes that Board Rule 207(b)(2) does not include the phrase "and vice versa," as recited in Board Rule 203(a).

Therefore according to Board Rule 207(b)(2), determination as to whether or not a claim corresponds to a count only requires a one-way test in which the count is deemed to be prior art to the claim in question.

(A) Designation of Claims Corresponding to Fordham Proposed Count 1

Claim 1 of UNM's '608 patent, and claims 60, 62, 63, 64, 78, 89, 90, and 92 of Fordham's above-captioned '754 application should be designated as corresponding to Fordham Proposed Count 1. **Appendix A** provides a claim chart that includes Fordham Proposed Count 1 as well as those claims of Fordham's above-identified application and UNM's '608 patent that should be designated as corresponding thereto.

Claim 1 of UNM's '608 patent recites a method of purification of hsp complexes in which the hsp is any hsp other than the heat shock protein species, hsp70 (*see* Section I(B)(2), above). Fordham Proposed Count 1 recites the same method of purification, but limits the hsp to one selected from the group consisting of hsp60, hsp65, rubisco binding protein, TCP-1, GroEL/GroES, Mif4, TCPalpha, TCPbeta, hsp104, hsp105, hsp110, DnaK, Ssa, Ssb, Ssc, hsp70, Grp75, Grp78(BiP), hsp90, gp96, and grp94. Since each of the heat shock protein species recited in this group falls within the scope of the genus recited in claim 1 of UNM's '608 patent, that claim would be anticipated by Fordham Proposed Count 1, where that count was deemed to be in the prior art. Even if claim 1 of UNM's '608 patent were to be deemed not to be anticipated by Fordham Proposed Count 1, it would be obvious over Fordham Proposed Count 1 for the reasons provided, *inter alia*, in Section II (D)(2), above.

Moreover, as demonstrated in Section II (D) above, claim 1 of UNM's '608 patent and claim 62 of Fordham's above-captioned application define interfering subject matter and are directed toward the same patentable invention; accordingly, claim 1 of UNM's '608 patent is anticipated by or is obvious over Fordham Proposed Count 1, which is defined in part as Fordham claim 62. Accordingly, claim 1 of UNM's '608 patent should be designated as corresponding to Fordham Proposed Count 1.

Fordham Proposed Count 1 is defined, in part, as Fordham claim 62. Accordingly, Fordham claim 62 would also be designated as corresponding to Fordham Proposed Count 1 under the standard provided by Board Rule 207(b)(2), *i.e.* Fordham Claim 62

would anticipate itself if it were in the prior art.

Count 1 of Interference 104,761 was defined, in part as Fordham claim 62. Fordham claims 60, 63, 64, 78, 89, 90, and 92 of Fordham's above-captioned application were designated, without objection, to correspond to Count 1 of Interference 104,761. Accordingly, claims 60, 63, 64, 78, 89, 90, and 92 should also be designated as corresponding to Fordham proposed Count 1, which is also defined in part as Fordham claim 62.

(B) Designation of Claims Corresponding to Fordham Proposed Count 2

Claim 2 of UNM's '608 patent, and claims 65, 66, 67, 79, 80, and 93 of Fordham's above-captioned '754 application should be designated as corresponding to Fordham Proposed Count 2. **Appendix B** provides a claim chart that includes Fordham Proposed Count 2 as well as those claims of Fordham's above-identified application and UNM's '608 patent that should be designated as corresponding thereto.

Claim 2 of UNM's '608 patent recites a method of synthesis of hsp complexes in which the hsp is any hsp other than the heat shock protein species, hsp70 (*see* Section I(B)(2), above). Fordham Proposed Count 2 recites the same method of synthesis, but limits the hsp to one selected from the group consisting of hsp60, hsp65, rubisco binding protein, TCP-1, GroEL/GroES, Mif4, TCPalpha, TCPbeta, hsp104, hsp105, hsp110, DnaK, Ssa, Ssb, Ssc, hsp70, Grp75, Grp78(BiP), hsp90, gp96, and grp94. Since each of the heat shock protein species recited in this group falls within the scope of the genus recited in claim 2 of UNM's '608 patent, that claim would be anticipated by Fordham Proposed Count 2, where that count was deemed to be in the prior art. Even if claim 2 of UNM's '608 patent were to be deemed not to be anticipated by Fordham Proposed Count 2, it would be obvious over Fordham Proposed Count 2 for the reasons provided, *inter alia*, in Section II (E)(2), above.

Moreover, as demonstrated in Section II (E) above, claim 2 of UNM's '608 patent and claim 65 of Fordham's above-captioned application define interfering subject matter and are directed toward the same patentable invention; accordingly, claim 2 of UNM's '608 patent is anticipated by or is obvious Fordham claim 65. Since Fordham Proposed Count 2 is defined, in

part by a broadened version of claim 65 [9], claim 2 of UNM's '608 patent would be anticipated by or be obvious over Fordham Proposed Count 2. Accordingly, claim 2 of UNM's '608 patent should be designated as corresponding to Fordham Proposed Count 2.

Fordham Proposed Count 2 is defined, in part, as a broadened version of Fordham claim 65 that was amended to remove any implicit ordering of the synthesis steps. Fordham submits that Fordham claim 65 would be obvious over, if not anticipated by Fordham Proposed Count 2. Fordham claim 65 and Fordham Proposed Count 2 only differ with respect to an implicit ordering of the steps, which is not considered to be a patentably distinct difference. Moreover, Count 4(2) of Interference 104,761 was also defined in part as this amended version of Fordham claim 65, and Fordham claim 65 was designated as corresponding to Count 4(2) in that Interference. Accordingly, Fordham claim 65 should also be designated as corresponding to Fordham Proposed Count 2 under the standard provided by Board Rule 207(b)(2).

Fordham claims 65, 66, 67, 79, 80, and 93 of Fordham's above-identified application were designated, without objection, as corresponding to Count 4(2) of Interference 104,761 that, as noted above, is identical in part to Fordham Proposed Count 2. Accordingly, claims 65, 66, 67, 79, 80, and 93 of Fordham's above-identified application should be also be designated as corresponding to Fordham Proposed Count 2.

(C) Designation of Claims Corresponding to Fordham Proposed Count 3

Claim 3 of UNM's '608 patent, and claims 68, 69, 71-75, 82-88, 94, and 95 of Fordham's above-captioned '754 application should be designated as corresponding to Fordham Proposed Count 3. **Appendix C** provides a claim chart that includes Fordham Proposed Count 3 as well as those claims of Fordham's above-identified application and UNM's '608 patent that should be designated as corresponding thereto.

Claim 3 of UNM's '608 patent recites a ternary hsp-ADP-peptide complex in which the hsp is <u>any</u> hsp other than the heat shock protein species, hsp70 (*see* Section I(B)(2), above). Fordham Proposed Count 3 recites the same ternary complex, but limits the hsp to one selected from the group consisting of DnaK, Ssa, Ssb, Ssc, hsp70, Grp75, Grp78(BiP), hsp90, gp96, and grp94. Since each of the heat shock protein species recited in this group falls within

[9] Claim 65 was broadened to remove any implicit requirement for an ordering of the synthesis steps. Accordingly, this part Fordham Proposed Count 3 is identical to the analogous portion of Count 4(2) of Interference 104,761.

the scope of the genus recited in claim 3 of UNM's '608 patent, that claim would be anticipated by Fordham Proposed Count 3, where that count was deemed to be in the prior art. Even if claim 3 of UNM's '608 patent were to be deemed not to be anticipated by Fordham Proposed Count 3, it would be obvious over Fordham Proposed Count 3 for the reasons provided, *inter alia*, in Section II (F)(2), above.

Moreover, as demonstrated above in Section II (F) above, claim 3 of UNM's '608 patent and claim 68 of Fordham's above-captioned application define interfering subject matter and are directed toward the same patentable invention; accordingly, claim 3 of UNM's '608 patent is anticipated by or is obvious over Fordham Proposed Count 3, which is defined in part as Fordham claim 68. Consequently, claim 3 of UNM's '608 patent should be designated as corresponding to Fordham Proposed Count 3.

Fordham Proposed Count 3 is defined, in part, as Fordham claim 68. Accordingly, Fordham claim 68 should also be designated as corresponding to Fordham Proposed Count 3 under the standard provided by Board Rule 207(b)(2), *i.e.* Fordham Claim 68 would anticipate itself if it were in the prior art.

Fordham claims 68, 69, 71-75, 82-88, 94, and 95 of Fordham's above-captioned application were deemed, without objection to correspond to Count 3 of Interference 104,761. Accordingly, claims 68, 69, 71-75, 82-88, 94, and 95 should also be designated as corresponding to Fordham Proposed Count 3, which as noted above, is analogous to, but broader than, Count 3 of Interference 104,761.

V. FORDHAM IS ENTITLED TO BENEFIT OF THE SEPTEMBER 13, 1995, FILING DATE OF ITS PARENT '391 APPLICATION FOR A CONSTRUCTIVE REDUCTION TO PRACTICE THAT FALLS WITHIN THE SCOPE OF EACH OF FORDHAM PROPOSED COUNTS 1, 2, AND 3

Fordham was accorded the benefit of its parent '391 application and declared the senior party in Interference 104,761. UNM challenged this designation in UNM Preliminary Motion 3. The Board found that Fordham had support for an embodiment within the scope of each of the three counts of Interference 104,761, and, therefore, denied UNM Preliminary Motion 3 (Exhibit 18 at pages 38-39). Since Fordham's Proposed Counts 1-3 are analogous to, if not broader than counts 1-3 of Interference 104,761, it follows that Fordham is entitled to benefit

of the filing date of its '391 application for an embodiment falling within the scope of each of Fordham Proposed Counts 1, 2, and 3 which define the interfering subject matter. Notwithstanding this conclusion, the information below is provided in order to comply with the requirements of Board Rule 202.

In the context of an interference proceeding, for an application to be entitled to benefit of an earlier-filed application under 35 U.S.C. § 120, " 'the § 112, first paragraph requirements need only be met for an *embodiment* within the count' in the special situation where the count is drawn to a genus and the previously-filed application discloses only a species thereof." *Weil v Fritz* 572 F.2d 856, 866 n. 16 (CCPA 1978) (emphasis in the original, citation omitted).

Fordham's involved '754 application and its earlier-filed '391 parent application are identical. Since Fordham has disclosed, in a 35 U.S.C. § 112 compliant manner, at least one constructive reduction to practice that falls within the scope of each of Fordham's proposed counts, Fordham's above-identified '754 application is entitled to the benefit of the filing date of its earlier-filed '391 parent application.

Fordham's above-identified '754 application was filed on June 4, 1998, as a division of Fordham's earlier-filed application Serial No. 08/527,391 (the " '391 application") (Exhibit 22) which was filed on September 13, 1995. The specification of the '754 application as filed is identical to that of its earlier-filed parent, the '391 application.

A preliminary amendment (Exhibit 21) was filed on January 13, 1999, in connection with the '754 application. The preliminary amendment amended the specification at page 16, line 25, by actually incorporating material that had been incorporated by reference in Fordham's earlier-filed '391 application (Exhibit 21, at page 11, second full paragraph through and including the first two paragraphs of page 12; and at page 3, line 1 through line 2, page 4). The preliminary amendment filed on January 13, 1999, in connection with the '754 application also amended the specification at page 36, line 31, and at page 60, line 22, to recite an inherent property of the complex produced by the methods described at page 36, lines 25-32, and at page 60, line 5-25, respectively. This amendment did not introduce new matter and was entered by the Examiner (Exhibit 21, at page 12 fourth paragraph; at page 10, first full paragraph; and at page 11, first paragraph).

Fordham's earlier-filed '391 parent application discloses (1) the purification of hsp70-peptide complexes using an ADP-agarose column (Exhibit 22 at page 60, lines 5-25, and at page 25, lines 1-17), (2) the synthesis of hsp70-peptide complexes involving the co-incubation of purified hsp70, an antigenic molecule, and ADP (Exhibit 22, at page 36, lines 25-32), and (3) the purified complexes produced by the method of isolation and the method of synthesis disclosed in Fordham's earlier-filed '391 parent application that inherently produce hsp70-ADP-peptide complexes (Exhibit 22, at page 60, lines 5-25, and at page 25, lines 1-17 and at page 36, lines 25-32; and Exhibit 22, at page 60, lines 19-21 (*also see* Exhibit 21, at page 12 third paragraph; at page 4, lines 18-19; and at page 6, lines 5-7)). **Appendix D** provides a chart, pursuant to 37 C.F.R. § 41.202 (a)(6), demonstrating where in Fordham's parent '391 specification, support is found for a constructive reduction to practice within the scope of the interfering subject matter, as it is defined by Fordham's proposed Counts 1, 2, and 3).

The specification of the '391 application, as well as Fordham's above-identified '754 application that is a continuation of the '391 application, both disclose a constructive reduction to practice that is encompassed within the scope of each of Fordham's Proposed Counts. More specifically, purification of hsp70-peptide complexes on an ADP-agarose column is disclosed at page 60, lines 5-25 and at page 25, lines 1-17 of the '391 application (Exhibit 22). This embodiment falls within the scope of Fordham's Proposed Count 1.

Synthesis of hsp70-peptide complexes is disclosed at page 36, lines 25-32 of the '391 application (Exhibit 22). This embodiment of the synthesis of hsp70-peptide complexes falls within the scope of Fordham's Proposed Count 2.

Moreover, the method of purification of hsp70-peptide complexes (disclosed at page 60, lines 5-25 and at page 25, lines 1-17 of the '391 application (Exhibit 22)) and the method of synthesis of hsp70-peptide (disclosed at page 36, lines 25-32 of the '391 application (Exhibit 22)) both inherently produce hsp70-ADP-peptide complexes (Exhibit 22, at page 60, lines 5-25, and at page 25, lines 1-17; and at page 36, lines 25-32; Exhibit 21, at page 12 third paragraph; at page 4, lines 18-19; and at page 6, lines 5-7). Therefore, the hsp70-ADP-peptide ternary complexes so produced fall within the scope of Fordham's proposed Count 3.

Consequently, the specification of Fordham's earlier filed '391 application, as well as Fordham's above-identified application that is a continuation of the '391 application,

disclose an embodiment within the scope of each of the Counts of the present interference.

Fordham's claims have been found allowable by the PTO and therefore, the specification of Fordham's above-identified '754 application provides § 112 compliant written description and enablement of Fordham's allowed claims. Since the specification of Fordham's earlier-filed '391 application and Fordham's above-identified '754 application are the same, it follows that the '391 application also provides § 112 compliant written description and enablement of the subject matter of Fordham's involved claims.

Thus, Fordham's earlier-filed '391 application also provides 35 U.S.C. § 112 compliant written description support and enablement for an embodiment that falls within the scope of each of Fordham's Proposed Counts. Accordingly, Fordham's above-identified '754 application is entitled to the benefit of the filing date of Fordham's earlier-filed '391 application since the law only requires that for benefit under 35 U.S.C. § 120, " 'the § 112, first paragraph requirements need only be met for an *embodiment* within the count' in the special situation were the count is drawn to a genus and the previously-filed application discloses only a species thereof." *Weil v Fritz* 572 F.2d 856, 866 n. 16, 196 USPQ 600, 608 (CCPA 1978) (emphasis in the original, citation omitted).

Fordham emphasizes that Fordham's proposed Counts 1 and 2 are drawn, respectively, to methods for the purification and for the synthesis of a genus of complexes comprising *inter alia* a heat shock protein 70 and a peptide, and that Fordham proposed Count 3 is drawn to a genus of purified hsp70-ADP-peptide complexes. Therefore in view of the facts and reasons provided above, Fordham's above-identified application and its parent both describe at least one species falling within the scope of each of Fordham's Proposed Counts. Therefore, Fordham is entitled under §120 to the filing date of its earlier-filed '391 application since "the description requirement is satisfied if the benefit application discloses a single species within the count." (*Irikura v. Peterson* 18 USPQ 1362, 1367 (BPAI 1990).

VI. THE REQUESTED INTERFERENCE SHOULD BE DECLARED BECAUSE FORDHAM'S EFFECTIVE FILING DATE IS PRIOR TO THE EFFECTIVE FILING DATE OF UNM'S '608 PATENT FOR EACH OF PROPOSED COUNTS 1, 2, AND 3

For the reasons provided in **Section V**, above, Fordham is entitled to the benefit

of the September 13, 1995, filing date of Fordham's parent '391 application for an embodiment falling within the scope of each of Fordham's Proposed Counts 1-3. At best, UNM's '608 patent claims priority, ultimately, to UNM's '239 application, which was filed September 20, 1996.

Therefore UNM's alleged priority date is more than one year later than the effective filing date to which Fordham is entitled, as established in Interference 104,761 and as demonstrated in **Section V** above.

Moreover, Fordham's effective filing date is also seven months earlier than UNM's earliest asserted date of conception, *i.e.* April 22, 1996 (Exhibit 10). Accordingly, Fordham is the first inventor of the subject matter encompassed by claims 1-3 of UNM's '608 patent and an interference should be declared to establish that fact.

VII. FORDHAM'S CLAIM TO *PRIMA FACIE* ENTITLEMENT TO JUDGMENT MAY BE BASED ON UNPATENTABILITY OF THE INTERFERING SUBJECT MATTER TO THE PATENTEE

In a request for interference, unpatentability to the patentee of the subject matter proposed for the interference may be raised as a basis for an Fordham's *prima facie* entitlement to judgment. Specifically, the administrative history of former Rule 608 clearly indicates that the basis for an applicant's entitlement to the judgment may be unpatentability of the interfering subject matter to the patentee, and need not be priority of invention:

> Under § 1.608, the PTO will continue current practice (37 CFR 1.204(c)) of requiring an applicant seeking to provoke an interference with a patent to submit evidence which demonstrates that the applicant is prima facie entitled to a judgment relative to the patentee. Evidence would be submitted only when the earlier of the filing date or effective filing date of the application is more than three months after the earlier of the filing date or effective filing date under 35 U.S.C. 120 of the patent. The evidence may relate to patentability and need not be restricted to priority.
>
> 49 Fed. Reg. 48416, 48421 (Dec. 12, 1984) (emphasis added).

This has been confirmed by the Board in *Basmadjian v. Landry*, 1997 WL 1724431, 54 USPQ2d 1617, 1619 (Bd. Pat. App. & Interf. 2000):

> the evidence may relate to patentability and need not be restricted to priority. Notice of Final Rule, Patent Interference Proceedings, 49 Fed. Reg. 84816 [*sic*, 48416], 48421 col. 3 (Dec. 12, 1984) *reprinted in* 1050 Off. Gaz. Pat. Office 385,

390 col. 3 (Jan. 29, 1985). For example, an applicant can establish that it is entitled to judgment *vis-a-vis* a patentee based on a *prima facie* showing of the unpatentability of the invention to the patentee under the first paragraph of 35 U.S.C. Section 112, *e.g.*, that the patentee's specification is not enabling.

Thus, a request for interference presenting only *evidence of unpatentability* and an *explanation* why applicant is entitled to judgment over the patentee is sufficient basis for declaration of an interference.

VIII. CLAIMS 1-3 OF THE '608 PATENT ARE UNPATENTABLE TO UNM

The issued claims of the '608 patent are not patentable to UNM for the reasons provided below.

A. Claims 1, 2, and 3, of UNM's '608 Patent Are Not Patentable to UNM Pursuant to the Final Decision in Prior Interference 104,761

The Judgment in Interference 104,761 ordered, *inter alia*, that UNM was not entitled to a patent containing claims 1, 3-5, 7-12 of UNM's '332 patent, which are directed toward a method of isolating hsp-peptide complexes, and which were designated as corresponding to Count 1 of Interference 104,761.

The Board found that UNM was not entitled to a generic method (*i.e.* claim 1 of UNM's '332 patent, which encompasses the subject matter of claim 1 of UNM's '608 patent) for purifying heat shock protein complexes using an ADP-matrix. [10]

Interference 104,761 also established that UNM was not entitled to the more-narrowly-claimed methods recited in the dependent claims of UNM's '332 patent for isolating such complexes (*i.e.* claims 3-5 and 7-12 of UNM's '332 patent) where the heat shock protein is any one of the following species: hsp60, hsp65, rubisco binding protein, TCP-1, GroEL/GroES, Mif4, TCPalpha, TCPbeta, hsp104, hsp105, hsp110, DnaK, Ssa, Ssb, Ssc, hsp70, Grp75, Grp78(BiP), hsp90, gp96, and grp94.

Thus claims 3-5 and 7-12 of UNM's '332 patent are directed toward species that

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[10] Claim 1 of UNM's '332 patent recites: A method for purifying heat shock protein complexes comprising the steps of: adding a heat shock protein complex comprising a heat shock protein associated with at least one member of the group consisting of peptides, polypeptides, denatured proteins and antigens associated therewith to ADP matrix column containing an ADP matrix to bind the heat shock protein complexes to the ADP matrix; and adding a buffer containing ADP to the column to remove the heat shock protein complexes in an elution product.

anticipate claim 1 of UNM's '608 patent. Moreover, claim 1 of UNM's '608 patent is also unpatentable to UNM as a generic claim since Interference 104,761 ordered that UNM was not entitled the even-broader, analogous claim 1 of the '332 patent. Accordingly, claim 1 of UNM's '608 patent cannot be patentable to UNM in view of the Board's decision.

The Judgment in Interference 104,761 also ordered that UNM was not entitled to a patent containing claims 13, 15-17, and 19-23 of UNM's '332 patent, which are directed toward a method of synthesizing hsp-peptide complexes and which were designated as corresponding to Count 4(2) of Interference 104,761.

The Board found that UNM was not entitled to a generic method (*i.e.* claim 13 of UNM's '332 patent) for synthesizing heat shock protein complexes. [11]

Interference 104,761 also established that UNM was not entitled to the more-narrowly-claimed methods recited in the dependent claims of UNM's '332 patent for synthesizing such complexes (*i.e.* claims 15-17 and 19-23 of UNM's '332 patent) where the heat shock protein is any one of the following species: hsp60, hsp65, rubisco binding protein, TCP-1, GroEL/GroES, Mif4, TCPalpha, TCPbeta, hsp104, hsp105, hsp110, DnaK, Ssa, Ssb, Ssc, hsp70, Grp75, Grp78(BiP), hsp90, gp96, and grp94.

Therefore, claims 15-17 and 19-23 of UNM's '332 patent are directed toward species that anticipate claim 2 of UNM's '608 patent. Moreover, claim 2 of UNM's '608 patent is also unpatentable to UNM as a generic claim since Interference 104,761 ordered that UNM was not entitled the even-broader, analogous claim 13 of the '332 patent. Accordingly, claim 2 of UNM's '608 patent cannot be patentable to UNM in view of the Board's decision.

The Board ordered that UNM was not entitled to a patent containing claims 13-30 of UNM's '716 patent or claims 1-18 of UNM's '141 patent which were designated as corresponding to Count 3 of Interference 104,761.

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[11] Claim 13 of UNM's '332 patent recites: A method for synthesizing heat shock protein complexes comprising the steps of: adding a heat shock protein to an ADP matrix column to bind the heat shock protein; adding a complexing solution comprising a complexing agent selected from the group consisting of peptides, polypeptides, denatured proteins and antigens to the column to form a heat shock protein complex with the heat shock protein bound to the ADP matrix column; and adding a buffer containing ADP to the column to remove the heat shock protein complex in an elution product.

The Board had found that claims encompassing ternary complexes comprising ADP, a peptide, and a heat shock protein selected from the group consisting of DnaK, Ssa, Ssb, Ssc, Grp75, Grp78(BiP), hsp90, gp96, and grp94, are not patentable to UNM. That is, the Board determined that particular species of ternary hsp-ADP-peptide complexes, which are encompassed by claim 3 of UNM's '608 patent, are not patentable to UNM. Since claim 3 of UNM's '608 patent would be anticipated by each of these ternary hsp-ADP-peptide complexes, claim 3 of UNM's '608 patent cannot be patentable to UNM in view of the Board's decision.

B. Claims 1, 2, and 3 of UNM's '608 Patent are Unpatentable to UNM Under 35 U.S.C. § 112, First and Second Paragraphs

UNM's '608 patent includes a total of three claims. Independent claims 1 and 2 recite, respectively, a method of purifying and a method of synthesizing heat shock protein complexes, "wherein said heat shock protein complexes are non-hsp70 heat shock protein complexes." Independent claim 3 is directed toward an ADP-heat shock protein-peptide complex, "wherein said heat shock protein complex is a non-hsp70 heat shock protein complex."

As noted above, the Detailed Description of the '608 patent indicates that the term "hsp70" refers to the eukaryotic protein hsp70, which is a member of the hsp70 family. Accordingly, each of the claims of the '608 patent recites a proviso or "negative limitation" that excludes only the particular species of hsp recited, *i.e.* hsp70. That is, claims 1-3 of UNM's '608 patent do not exclude the entire hsp70 family of proteins, which includes, *inter alia*, DnaK proteins from prokaryotes; Ssa, Ssb, and Ssc from yeast; and Grp75 and Grp78(Bip) from eukaryotes (*see* the '608 patent, at column 4, lines 1-6) (*see* Section I(B)(2), above).

(1) Claims 1-3 of UNM's '608 Patent are Unpatentable to UNM Under the First Paragraph of § 112

Claims drafted with a negative limitation or proviso that is not supported by the specification as filed do not meet the written description requirement of 35 U.S.C. § 112, first paragraph (*In re Grasselli* 231 USPQ 393, 394 (Pat. & Tr. Office Bd. App. 1983)).

The specification of the '608 patent does not disclose a genus encompassing all heat shock proteins other than hsp70, as recited in each of the claims of the '608 patent. Rather, UNM's specification provides (1) two Examples, which are limited to purification of hsp70 complexes, and (2) a list of representative non-hsp70 heat shock proteins known in the art. No

explanation was provided as to why non-hsp70 complexes could not be isolated or synthesized according to the hsp70-related methods, nor was any guidance provided regarding any modification of the hsp70-related methods to enable them to be used for non-hsp70 complexes (Exhibit 18, ¶ 100 at page 20). Thus, UNM's specification had provided essentially no enabling details regarding any hsp other than hsp70, indicating that UNM was confident that those skilled in the art would be able to carry out the claimed methods involving non-hsp70 complexes in view of its disclosure of methods for the purification and synthesis of hsp70 complexes, without more (Exhibit 18; page 43, first paragraph). That is, according to the Board, "UNM apparently viewed the listed heat-shock proteins as an interchangeable class" for use in the claimed methods for purification and synthesis of hsp complexes (*Id.*).

Consequently, Claims 1-3 of UNM's '608 patent are unpatentable to UNM under 35 U.S.C. § 112, first paragraph, for lack of a written description of a genus comprising all heat shock proteins other than the heat shock protein species, hsp70 (*i.e.* the only species demonstrated to work in the Examples provided). Moreover, should UNM's disclosure of hsp70-related methods and a list of known heat shock proteins be deemed to provide written description support for claims 1-3 of UNM's '608 patent, then those claims would be obvious under 35 U.S.C. § 103, over § 102(g) prior art directed toward methods and complexes involving hsp70 (*see e.g.* Exhibit 18, page 42, last paragraph through the first paragraph at page 43).

(2) Claims 1-3 of UNM's '608 Patent are Unpatentable to UNM Under the Second Paragraph of § 112

Claims reciting a negative limitation or proviso are not inherently indefinite. Where a specification positively recites particular species or alternative elements of an invention, they may be explicitly excluded from the scope of a claim; *i.e.* a specification that discloses the whole necessarily describes the parts *In re Johnson* 558 F.2d 1008, 1019, 194 USPQ 187, 196 (CCPA 1977) (*also see* MPEP 2173.05(i)).

In *Johnson* the Court found that the applicants had narrowed their claims to avoid reading on those species lost in an interference, and that the new "limited genus" recited in the claims was supported both generically and by specific examples disclosed in the specification. The narrowed claims, in fact, encompassed fewer species and examples than were disclosed in the specification as filed. *In re Johnson* 558 F.2d 1008, 1018, 194 USPQ 187, 196 (CCPA

1977).

In contrast, claims have been rejected as indefinite under 35 U.S.C. § 112, second paragraph where they were drafted with a negative limitation or proviso that attempted to define the invention as encompassing all subject matter that has not been invented by others (*In re Schechter* 205 F.2d 185, 187-188, 98 USPQ 144, 147 (CCPA 1953). Such claims are unpatentable under § 112 because the inventor has failed to particularly point out and distinctly claim his invention. Instead, he has attempted to claim everything, whether known or unknown, except that which was disclosed in the prior art (*Id.*).

In view of *Johnson* and *Schechter*, it is apparent that the three independent claims of the '608 patent are indefinite under 35 U.S.C. § 112, second paragraph. Claims 1-3 of UNM's '608 patent do not "particularly point out and distinctly claim" UNM's alleged invention. Rather, each attempts to define an invention that encompasses all heat shock protein complexes other than those including the species hsp70; *i.e.* each attempts to claim everything other than prior art (at least as it was narrowly, and incorrectly, perceived by UNM; *i.e. see* Exhibit 18, at page 37, and the following Section).

C. Claims 1, 2, and 3 of UNM's '608 Patent Were Issued in Contradiction to the Provisions of Former 37 C.F.R. § 1.658(c) and Current 37 C.F.R. § 41.127(a) Regarding Interference Estoppel

Former 37 C.F.R. § 1.658(c), which was in effect while UNM prosecuted the '418 application, provides:

> A judgment in an interference settles all issues which (1) were raised and decided in the interference, (2) could have been properly raised and decided in the interference by a motion under § 1.633 (a) through (d) and (f) through (j) or § 1.634, and (3) could have been raised and decided in an additional interference with a motion under § 1.633(e). A losing party who could have properly moved, but failed to move, under §§ 1.633 or 1.634, shall be estopped to take ex parte or inter parties action in the Patent and Trademark Office after the interference which is inconsistent with that party's failure to properly move

Current Board Rule 127(a) provides

> A judgment disposes of all issues that were, or by motion could have properly been, raised an decided. A losing party who could have properly moved for relief on an issue, but did not so move, may not take action in the Office after the judgment that is inconsistent with that party's failure to move, except that a losing

party shall not be estopped with respect to any contested subject matter for which that party was awarded a favorable judgment.

The decision in Interference 104,761 was adverse to UNM with respect to the three counts of that interference, and, therefore, under both former Rule 1.658(c) as well as under new Board Rule 127(a), UNM was estopped with respect to *ex parte* prosecution of any claim that would correspond to a count of Interference 104,761. Therefore, according to that decision, UNM was not entitled to its claims corresponding to count 1 (*i.e.* claims 1, 3-5, and 7-12 of UNM's '332 patent), count 2 (*i.e.* claims 13, 15-17, and 19-23 of UNM's '332 patent), and count 3 (*i.e.* claims 13-30 of UNM's '716 patent and claims 1-18 of UNM's '141 patent)

Nevertheless, even after the entry of the final judgment, which was not appealed by either party and is now final, UNM continued to take *ex parte* action in the PTO with respect to claims 1-3 of UNM's '608 patent, even though UNM clearly should have known that those claims would have corresponded to each of the lost counts.

For example, claims 1 and 13 of UNM's '332 patent, are broader than claims 1 and 2, respectively, of UNM's '608 patent. Moreover, claims 8-11 of the '332 patent recite a total of 19 species falling within the scope of claim 1 of UNM's '608 patent, while claims 20-23 of UNM's '332 patent recite a total of 19 species falling within the scope of claim 2 of UNM's '608 patent. Similarly, claims 13-30 of UNM's '716 patent, and claims 1-18 of UNM's '141 patent, collectively, recite a total of nine species falling within the scope of claim 3 of UNM's '608 patent.

It should have been apparent to UNM upon declaration of Interference 104,761 and upon UNM's review of Fordham's allowed claims in the above-captioned application, that the claims UNM prosecuted and allowed in both UNM's '141 and '608 patents were not patentably distinct from the counts of Interference 104,761.

Even more specifically, the conclusion that UNM was estopped from prosecuting the pending claims of its '418 application should have been apparent to UNM by August 18, 2003, when the Decision on Motions was issued by the Board. In fact, any questions regarding the separate patentability of claims reciting complexes comprising any hsp "other than hsp70" were explicitly answered by the Board at page 37 of the Decision on Motions in Interference 104,761 (Exhibit 18):

> While broader claims that are not limited to hsp70 family heat-shock proteins are designated as corresponding to the count, this designation simply reflects the fact that the broader claims would be anticipated by priority proofs to the narrower subject matter of the counts. It is long and well established that loss of narrower subject matter in an interference bars a losing party from claiming broader subject matter encompassing the lost count absent (absent a sufficient antedating effort for the generic subject matter). E.g., In re Zletz, 893 F.2d 319, 322-23, 13 USPQ2d 1320, 1322-23 (Fed. Cir. 1989); In re Kyrides, 159 F.2d 1019, 1022, 73 USPQ 61, 63 (CCPA 1947).

Nevertheless, UNM drafted and prosecuted claims that were patentably indistinct from the three counts of then-pending Interference 104,761, and that clearly encompassed subject matter lost in that interference, without ever notifying the Examiner of either the judgment, or even the existence, of Interference 104,761.

D. Claims 1, 2, and 3 of UNM's '608 Patent Are Unpatentable to UNM Under 35 U.S.C. §§ 102(g) and 103 Over the Subject Matter of Counts 1-3 of Interference 104,761

The subject matter of the three counts of Interference 104,761 is § 102(g) and/or § 103 prior art with respect to UNM's '418 application. *In re Risse* 378 F.2d 948, 957, 154 USPQ 1, 8 (CCPA 1967) (*overruled on other grounds*). Accordingly, the claims prosecuted by UNM in the '418 application were required to be inventively different over the counts of Interference 104,761 in order to be considered patentable. In fact, on August 18, 2003, in Interference 104,761, the Board explicitly notified UNM that claims reciting non-hsp70 species as well as generic claims encompassing heat shock proteins without limitation to a family or species, were not patentably distinct over the counts (*see* the Board's Decision on Motions in Interference 104,761, Exhibit 18, at page 37, quoted in the previous section). On this basis alone, it is apparent that claims 1-3 of UNM's '608 patent are not patentable to UNM over the counts of Interference 104,761.

The three counts established in Interference 104,761 were defined, in the alternative as claim 10 of UNM's '332 patent, claim 22 of UNM's '332 patent, and claims 13, 19, and 25 of UNM's '716 patent. Moreover, claims 1, 3-5, and 7-12 of UNM's '332 patent were designated as corresponding to Count 1 of Interference 104,761, claims 13, 15-17, and 19-23 of UNM's '332 patent were designated as corresponding to Count 4(2) of Interference

104,761, and claims 13-30 of UNM's '716 patent and claims 1-18 of UNM's '141 patent were designated as corresponding to Count 3 of Interference 104,761.

(1) Prosecution History of UNM's '418 Application

In the Office Action issued December 13, 2002 (Exhibit 20), the Examiner rejected pending claims 24-26 of UNM's '418 application (which ultimately issued as claims 1-3, respectively, of UNM's '608 patent) under the judicially-created doctrine of obviousness-type double patenting over issued claims in UNM's '332, '141, and '716 patents. The Examiner found that pending claims 24 and 25 were not patentably distinct over claims 1-23 of UNM's '332 patent, and that pending claim 26 was not patentably distinct over claims 1-30 of UNM's '716 patent and claims 1-18 of UNM's '141 patent.

Thus, the U.S. Patent and Trademark Office had determined that claims 1-3 of UNM's '608 patent were not patentably distinct over subject matter that is, in fact, § 102(g) and/or § 103 prior art against UNM.

(2) Claim 1 of UNM's '608 Patent is Not Patentable to UNM Over Count 1 of Interference 104,761

Claim 1 of UNM's '608 patent recites the following:

> A method for purifying heat shock protein complexes comprising the steps of:
>
> adding a solution containing heat shock protein complex associated with at least one member of the group consisting of peptides, polypeptides, denatured proteins and antigens to an ADP matrix column containing an ADP matrix to bind the heat shock proteins complexes to the ADP matrix; and
>
> adding a buffer containing ADP to the column to remove the heat shock protein complexes in an elution product, wherein said heat shock protein complexes are non-hsp70 heat shock protein complexes.

Count 1 of Interference 104,761 was defined as the method of claim 10 of UNM's OR that of Claim 62 of Fordham. Claim 10 of UNM's '332 patent recites the following:

> The method of claim 1 [A method for purifying heat shock protein complexes comprising

the steps of:

adding a heat shock protein complex comprising a heat shock protein associated with at least one member of the group consisting of peptides, polypeptides, denatured proteins and antigens associated therewith to ADP matrix column containing an ADP matrix to bind the heat shock protein complexes to the ADP matrix; and

adding a buffer containing ADP to the column to remove the heat shock protein complexes in an elution product.]

wherein the heat shock protein complexes include complexes in which the heat shock protein comprises one of the group consisting of DnaK proteins from prokaryotes; Ssa, Ssb, and Ssc from yeast; hsp70, Grp75 and Grp78 (Bip) from eukaryotes.

OR

Claim 62 of Fordham's above-identified application, which recites the following:

A method for purifying heat shock protein 70 complexes, comprising the steps of:

adding a solution containing a heat shock protein 70 complex comprising a heat shock protein 70 associated with at least one member of the group consisting of peptides and proteins, to an ADP matrix column containing and ADP matrix to bind the heat shock protein 70 complexes to the ADP matrix; and

adding a buffer containing ADP to the column to remove the heat shock protein 70 complexes in an elution product.

Count 1 of Interference 104,761 recites six species falling within the scope of Claim 1 of UNM's '608 patent. Thus, Claim 1 of UNM's '608 patent is anticipated by Count 1 of Interference 104,761 which recites, in the alternative, the same method of purification of heat shock protein complexes in which the hsp is selected from the group consisting of DnaK, Ssa, Ssb, Ssc, Grp75, and Grp78 (Bip), in addition to hsp70.

Moreover, even if, for the sake of argument only, Claim 1 of UNM's '608 patent

were deemed not to be anticipated, that claim would nevertheless be obvious under § 103 over Count 1 of Interference 104,761. Count 1 is directed, in the alternative to a method for the purification of hsp complexes in which the hsp is either a member of the hsp70 family or, more specifically, the hsp is selected from the group consisting of DnaK, Ssa, Ssb, Ssc, Grp75, Grp78 (Bip), and hsp70.

As noted above in Sections II (A)(1), (2), and (4), heat shock proteins share two fundamental activities: the ability to bind peptides and the ability to bind adenine nucleotides. The demonstration that hsp complexes could be purified according the method of Count 1 of Interference 104,761 would establish that stable, ternary, column-bound hsp-ADP-peptide complexes could form, and that such complexes could be eluted with a solution comprising ADP. Accordingly, in view of these observations, it would have been obvious to those of ordinary skill that other non-hsp70-family-member heat shock proteins could be substituted for the hsp70 family member, with a reasonable expectation of success, since the method relied upon traits common to both hsp70 family members and non-hsp70-family-member heat shock proteins, such as *e.g.* hsp90 or gp96 (*also see* Exhibit 18, at page 37, second paragraph, and at page 43, first paragraph).

As noted above in Section II(A)(3), motivation for substituting a non-hsp70-family-member heat shock protein (such as hsp90 or gp96) in the method of Count 1, was provided (1) by the expectation that such complexes might be useful for the prevention or treatment of cancer and infectious disease, and (2) by the recognition that available methods for purification of immunogenic complexes were either less efficient or did not provide the desired hsp-peptide complexes.

(3) Claim 2 of UNM's '608 Patent is Not Patentable to UNM Over Count 4(2) of Interference 104,761

Claim 2 of UNM's '608 patent recites the following:

> A method for synthesizing heat shock protein complexes comprising the steps of:
>
> adding a solution containing a heat shock protein to an ADP matrix column containing an ADP matrix to bind the heat shock protein to the ADP matrix;
>
> adding a complexing solution comprising a complexing agent selected from the group

consisting of peptides, polypeptides, denatured proteins and antigens to the column to form heat shock protein complexes with the heat shock protein bound to the ADP matrix column; and

adding a buffer containing ADP to the column to remove the heat shock protein complexes in an elution product, wherein said heat shock protein complexes are non-hsp70 heat shock protein complexes.

Count 4(2) of Interference 104,761 was defined as the method of claim 22 of UNM's '332 patent or as Fordham proposed claim 96, a modification of Fordham claim 65. Claim 22 of UNM's '332 patent recites the following:

The method of claim 13 [A method for synthesizing heat shock protein complexes comprising the steps of:

adding a heat shock protein to an ADP matrix column to bind the heat shock protein;

adding a complexing solution comprising a complexing agent selected from the group consisting of peptides, polypeptides, denatured proteins and antigens to the column to form a heat shock protein complex with the heat shock protein bound to the ADP matrix column; and

adding a buffer containing ADP to the column to remove the heat shock protein complex in an elution product]

wherein the heat shock protein complexes include complexes in which the heat shock protein comprises one of the group consisting of DnaK proteins from prokaryotes; Ssa, Ssb, and Ssc from yeast; hsp70, Grp75 and Grp78(Bip) from eukaryotes.

OR

Claim 96 of Fordham, which recites the following:

A method of synthesizing heat shock protein 70 complexes, comprising contacting a heat shock protein 70 with an antigenic molecule selected from the group consisting of peptides and proteins, and with a buffer containing ADP to allow the heat shock protein

70 to bind the antigenic molecule and to allow the heat shock protein 70 to bind to the ADP to form a heat shock protein 70 complex.

Count 4(2) of Interference 104,761 recites six species falling within the scope of Claim 2 of UNM's '608 patent. Thus, Claim 2 of UNM's '608 patent is anticipated by Count 4(2) of Interference 104,761 which recites, in the alternative, the same method of synthesis of heat shock protein complexes in which the hsp is selected from the group consisting of DnaK, Ssa, Ssb, Ssc, Grp75, and Grp78 (Bip), in addition to hsp70.

Moreover, even if, for the sake of argument only, Claim 2 of UNM's '608 patent were deemed not to be anticipated, that claim would nevertheless be obvious under § 103 over Count 4(2) of Interference 104,761. Count 4(2) is directed, in the alternative to a method for the synthesis of hsp complexes in which the hsp is either a member of the hsp70 family or, more specifically, the hsp is selected from the group consisting of DnaK, Ssa, Ssb, Ssc, Grp75, Grp78 (Bip), and hsp70. As noted above in Sections II(A)(1), (2), and (4), heat shock proteins share two fundamental activities: the ability to bind peptides and the ability to bind adenine nucleotides. The demonstration that hsp complexes could be synthesized according the method of Count 4(2) of Interference 104,761 would establish that stable, ternary, hsp-ADP-peptide complexes could be synthesized by combining ADP, a peptide, and an hsp, wherein the hsp is a member of the hsp70 family. Accordingly, in view of these observations, it would have been obvious to those of ordinary skill that other non-hsp70-family-member heat shock proteins could be substituted for the hsp70 family member with a reasonable expectation of success since the method relied upon traits common to both hsp70 family members and non-hsp70-family-member heat shock proteins (*e.g.* hsp90 or gp96); (*also see* Exhibit 18, at page 37, second paragraph, and at page 43, first paragraph).

As noted above in Section II(A)(3), motivation for substituting a non-hsp70-family-member heat shock protein, such as hsp90 or gp96, in the method of Count 4(2), with a reasonable expectation of success, was provided by the realization that such complexes might be useful for the prevention or treatment of cancer and infectious disease.

(4) Claim 3 of UNM's '608 Patent is Not Patentable to UNM Over Count 3 of Interference 104,761

Claim 3 of UNM's '608 patent recites the following:

An ADP-heat shock protein-peptide complex in purified form, wherein said heat shock protein complex is a non-hsp70 heat shock protein complex.

Count 3 of Interference 104,761 is the ADP-heat shock protein-peptide complex of claims 13, 19, or 25 of UNM's '716 patent which recite the following:

13. A purified ADP-heat shock protein-peptide complex, wherein said heat shock protein is selected from the group consisting of DnaK proteins from prokaryotes.

19. A purified ADP-heat shock protein-peptide complex, wherein said heat shock protein is selected from the group consisting of Ssa, Ssb, and Ssc from yeast.

25. A purified ADP-heat shock protein-peptide complex, wherein said heat shock protein is selected from the group consisting of Grp75 and Grp78(Bip) from eukaryotes.

Count 3 of Interference 104,761 recites six species falling within the scope of Claim 3 of UNM's '608 patent. Thus, Claim 3 of UNM's '608 patent is anticipated by Count 3 of Interference 104,761 which recites ternary hsp-ADP-peptide complexes in which the shock protein is selected from the group consisting of DnaK, Ssa, Ssb, Ssc, Grp75, and Grp78 (Bip).

Moreover, even if, for the sake of argument only, Claim 3 of UNM's '608 patent were deemed not to be anticipated, that claim would nevertheless be obvious under § 103 over Count 3 of Interference 104,761. Count 3 is directed toward hsp-ADP-peptide complexes in which the hsp is selected from the group consisting of DnaK, Ssa, Ssb, Ssc, Grp75, Grp78 (Bip), and hsp70. As noted above in Sections II (A)(1), (2), and (4), heat shock proteins share two fundamental activities: the ability to bind peptides and the ability to bind adenine nucleotides. In view of the demonstration that stable ternary hsp-ADP-peptide complexes existed, as recited in Count 3 of Interference 104,761, it would have been obvious to those of ordinary skill that other non-hsp70-family-member heat shock proteins could be substituted for the hsp70 family member with a reasonable expectation of success since the existence and stability of those ternary complexes was a reflection of these two fundamental activities common to both hsp70 family members and non-hsp70-family-member heat shock proteins, such as *e.g.* hsp90 or gp96 (*also see* Exhibit 18, at page 37, second paragraph, and at page 43, first paragraph).

As noted above in Section II (A)(3), motivation for substituting a

non-hsp70-family-member heat shock protein, such as hsp90 or gp96, in the complexes of Count 3 of Interference 104,761, was provided by the expectation that such complexes might be useful for the prevention or treatment of cancer and infectious disease.

(5) Claims 1-3 of UNM's '608 Patent Are Unpatentable to UNM under 35 U.S.C. §§ 102(g) and 103

For the reasons provided in preceding sections (1)-(4), it is apparent that claims 1-3 of UNM's '608 patent are not inventively different over the counts of Interference 104,761. Consequently, claims 1-3 of UNM's '608 patent are not patentable to UNM under 35 U.S.C. §§ 102(g) and 103 (*In re Risse* 378 F.2d 948, 957 154 USPQ 1, 8 (CCPA 1967)).

E. UNM's '608 Patent Is Unenforceable As a Result of UNM's Inequitable Conduct During Prosecution of the '418 Application Which Issued as UNM's '608 Patent

37 C.F.R. § 1.56 (a) provides, in part, that

> Each individual associated with the filing and prosecution of a patent application has a duty of candor and good faith in dealing with the Office, which includes a duty to disclose to the Office all information known to that individual to be material to patentability.

Section (b) of Rule 56 further provides that information is material to patentability if "it establishes, by itself or in combination with other information, a prima facie case of unpatentability of a claim." In addition, "[i]nformation is 'material' where there is a substantial likelihood that a reasonable examiner would have considered the information important in deciding whether to allow the application to issue as a patent" *Molins PLC v. Textron, Inc.* 48 F.3d 1172, 1179, 33 USPQ2d 1823, 1827 (Fed. Cir. 1995). The test for materiality, therefore, "is whether a reasonable examiner would have considered the information important, not whether the information would conclusively decide the issue of patentability." *The Li Second Family Limited Partnership v. Toshiba Corporation* 231 F.3d. 1373, 1380, 56 USPQ2d 1681, 1687 (Fed. Cir. 2000).

Accordingly, "[a]pplicants for patents are required to prosecute patent applications in the PTO with candor, good faith, and honesty" and "a breach of this duty

constitutes inequitable conduct." *Molins PLC v. Textron, Inc.* 48 F.3d 1172, 1178, 33 USPQ2d 1823, 1826 (Fed. Cir. 1995) (citations omitted). In this context, the term "applicants" encompasses the inventor as well "each attorney who prepares or prosecutes an application and on every other individual who is substantively involved in the preparation or prosecution of the application and who is associated with the inventor, with the assignee, or with anyone to whom there is an obligation to assign the application." (*Id.* Fn. 6)

Inequitable conduct encompasses not only affirmative misrepresentations of material fact, but also failure to disclose material information, in conjunction with an intent to deceive *Baxter International v. McGaw Inc.* 149 F.3d 1321, 1327, 47 USPQ2d 1225, 1229 (Fed. Cir. 1998) (citation omitted). Where inequitable conduct can be inferred, "lapse on the part of the Examiner does not excuse the applicant" *Kangaroos U.S.A., Inc. v. Caldor, Inc.* 778 F.2d 1571, 1576, 228 USPQ 32, 35 (Fed. Cir. 1985) (citation omitted). Indeed "[t]here is no reprieve from the duty of square dealing and full disclosure that rests on the patent practitioner in dealings with the PTO ... this duty is not done by one who knowingly takes advantage of an error by the PTO." (*Id.*).

In order to establish the existence of inequitable conduct based upon a failure to disclose information to the PTO, the following must be established, by clear and convincing proof: (1) that the withheld information was material, (2) that there was knowledge chargeable to the applicant of both the existence and the materiality of that information, and (3) that failure to disclose the information was the result of an intent to mislead the PTO. *FMC Corporation v. The Manitowoc Company, Inc.* 835 F.2d 1411, 1415, 5 USPQ2d 1112, 1115 (Fed. Cir. 1987).

However, direct evidence is not required to establish an intent to mislead; typically, it is inferred from the facts. Furthermore, the "more material the information misrepresented or withheld by the applicant, the less evidence of intent will be required in order to find that inequitable conduct has occurred." *The Li Second Family Limited Partnership v. Toshiba Corporation* 231 F.3d. 1373, 1378, 56 USPQ2d 1681, 1687 (Fed. Cir. 2000).

In fact, "intent may be inferred when a patent applicant knew or should have known, that withheld information could be material to the PTO's consideration of the patent application" and, in such instances the patentee "may expect to have great difficulty in establishing subjective good faith sufficient to overcome an inference of intent to mislead."

Bristol-Myers Squibb v. Rhone-Poulenc Rorer 326 F.3d 1226, 1239, 66 USPQ2d 1481, 1490 (Fed. Cir. 2003); (*also see Critikon, Inc. v. Becton Dickinson Vascular Access, Inc.* 120 F.3d 1253, 1256, 43 USPQ2d 1666, 1668 (Fed. Cir. 1997); "intent may be inferred where a patent applicant knew, or should have known, that withheld information would be material to the PTO's consideration of the patent application").

Thus, although a demonstration of subjective good faith may offset some degree of materiality, "a determination of inequitable conduct will not be avoided if knowledge of materiality or gross negligence greatly outweighs the lack of deceptive intent. Where an applicant or his attorney knew or should have known that a reference was material, (*see* Rule 56(a)), the failure to disclose the reference is sufficient to establish intent." *A.B. Dick Company v. Burroughs Corporation* 798 F.2d 1392, 1398, 230 USPQ 849, 854 (Fed. Cir. 1986).

Inequitable conduct has been found under circumstances analogous to UNM's prosecution of the '418 application. That is, inequitable conduct was found where an applicant was simultaneously prosecuting two sibling applications that were being reviewed by two different examiners, and a material determination regarding the first application was never communicated to the second examiner. More specifically, during prosecution of the first application, the examiner denied applicant's claim to the benefit of the filing date of an earlier application. This denial was appealed to the PTO Board of Appeals, which also rejected applicant's attempt to establish the earlier priority date. *The Li Second Family Limited Partnership v. Toshiba Corporation* 231 F.3d. 1373, 1376-1377, 56 USPQ2d 1681, 1683 (Fed. Cir. 2000). Despite this result, the applicant not only failed to communicate this adverse decision of the Board to the second examiner, but the applicant also continued to rely upon that priority claim, to which the applicant knew it was not entitled, while continuing to prosecute the subject application (*Li* at 1378).

Fordham submits that UNM failed to inform the Examiner of the very existence of the ongoing Interference 104,761, much less the Board's adverse decisions in that interference, for over two years during prosecution of both the '418 application, which issued as UNM's '608 patent as well as during prosecution of the '381 application which issued as UNM's '141 patent. Moreover, Fordham submits that UNM's earlier prosecution of its '381 application that issued as UNM's '141 patent and that was subsequently included within Interference

104,761, would rebut any suggestion by UNM that it was unaware of the nature of its conduct during the even-later filing and prosecution of its '418 application.

UNM's prosecution of the '418 application, which issued as UNM' '608 patent, should be deemed to be inequitable conduct on the part of UNM. Fordham submits that the withheld information was irrefutably material to the Examiner's determination of the patentability of UNM's pending claims, and that UNM is chargeable with both knowledge of this information and its materiality.

Therefore, Fordham submits that it can be inferred from all the facts and circumstances surrounding prosecution of the '418 application that UNM took advantage of the Examiner's lack of awareness of Interference 104,761 and intended to mislead the PTO, particularly in view of (1) the materiality of the information UNM withheld from the Examiner, and (2) the explicit determination both by the Examiner and the Board that UNM was not entitled to the claims it continued to prosecute.

The existence of the ongoing Interference 104,761 and the decisions reached by the Board were material to the patentability of UNM's pending claims in the '418 application since "the losing party cannot obtain claims to subject matter which is either barred under 35 U.S.C. § 102(g), or rendered obvious under 35 U.S.C. § 103, by the invention defined in the counts" *In re Risse* 378 F.2d 948, 957, 154 USPQ 1, 8 (CCPA 1967) (*overruled on other grounds*). *Risse* provides that the subject matter of the interference counts is encompassed within prior invention under 35 U.S.C. § 102(g) and may be used as prior art under § 103. Accordingly, claims asserted by the losing party in an interference must be inventively different from the counts of the interference in order to be considered patentable (*Id.* at 1505).

The existence of the ongoing Interference 104,761 and the decision reached by the Board were material to the patentability of UNM's pending claims in the '418 application since, under the settled principles of collateral estoppel and *res judicata*, the decision of the Board in Interference 104,761 barred UNM "from obtaining a patent for claims that are patentably indistinguishable" from those lost in the interference (*In re Deckler* 977 F.2d 1449, 1452, 24 USPQ2d, 1448, 1449 (Fed. Cir. 1992). This should have been apparent to UNM since interference estoppel has been applied by the Federal Circuit "to bar the assertion of claims for inventions that are patentably indistinct from those in an interference that the applicant has lost"

(*Id.*, citing *In re Kroekel*, 803 F.2d 705, 231 USPQ 640 (Fed. Cir. 1986) and *Woods v. Tsuchiya* 754 F.2d 1571, 225 USPQ 11 (Fed. Cir. 1985)). In fact, UNM had been notified by the Examiner in the Office Action of December 13, 2002, that UNM's pending claims in the '418 application were not patentably distinct (a) over claims defined as counts in Interference 104,761, and/or (b) over claims designated as corresponding to the counts of Interference 104,761.

Former Rule 658 (which was in effect while UNM prosecuted the '418 application) incorporated the above holdings and provided, in section (c) that:

> A judgment in an interference settles all issues which (1) were raised and decided in the interference, (2) could have been properly raised and decided in the interference by a motion under § 1.633 (a) through (d) and (f) through (j) or § 1.634 and (3) could have been properly raised and decided in an additional interference with a motion under § 1.633(e). A losing party who could have properly moved, but failed to move, under §§ 1.633 or 1.634 shall be estopped to take ex parte or inter parties action in the Patent and Trademark Office after the interference which is inconsistent with that party's failure to properly move, except that a losing party shall not be estopped with respect to any claims which correspond, or properly could have corresponded to a count as to which that party was awarded a favorable judgment.

As noted herein, on October 12, 2001, Interference 104,761 was declared between the above-captioned application and UNM's '332 patent (with two counts directed toward purification and synthesis of hsp complexes, the subject matter of claims 1 and 2 of UNM's '608 patent). Interference 104,761 was redeclared to include UNM's '716 patent and to add a third count that was directed toward ternary hsp-ADP-peptide complexes, the subject matter of claim 3 of UNM's '608 patent). Interference 104,761 was redeclared a second time to include UNM's '141 patent, which UNM had prosecuted in parallel with the ongoing Interference 104,761.

Moreover, UNM filed the '418 application eight months after Interference 104,761 had been declared and, again, prosecuted this application in parallel with the ongoing interference. The '418 application issued as UNM's '608 patent on March 30, 2004, five months after the final decision in Interference 104,761 had been issued, *i.e.* after that decision had become final and after the time for appeal thereof had passed.

Therefore, during a period of almost two and one-half years after Interference

104,761 was declared, UNM continued to prosecute two patent applications with claims that were not patentably distinct from the three counts of Interference 104,761. At the least, UNM should have known that the claims of the pending '418 application, which issued as UNM's '608 patent, were directed toward patentably indistinct subject matter in view of: (1) the Board's decision on the preliminary motions (Exhibit 18) and (2) their final decision (Exhibit 7) in Interference 104,761, as well as (3) the Examiner's rejection of the pending claims of the '418 application under the judicially-created doctrine of obviousness-type double patenting (Exhibit 20). In that rejection the Examiner explicitly found that UNM's pending claims were not patentably distinct from claims of UNM's '332, '716, and '141 patents (which patents were all involved in Interference 104,761), including those claims either defined as a count in Interference 104,761 or designated as corresponding to a count of that pending interference.

Accordingly, in view of the Examiner's determination, and in light of the provisions of Rule 658(c), Fordham submits that a reasonable examiner would have considered the very existence of Interference 104,761, as well as the decisions reached by the Board in that interference, to be material to a determination of the patentability of UNM's pending claims in the '418 application.

In view of the ongoing Interference, the two pending applications, the redeclaration of the interference to include all three of the patents to which the '418 application claimed priority, the caselaw cited above, and the requirements of Rule 658, UNM cannot argue that it was unaware of the materiality of this information. UNM cannot suggest that a reasonable examiner would not have considered the existence of and the decisions reached in Interference 104,761 to be important when considering the patentability of UNM's pending claims. This is particularly evident with respect to the particular Examiner reviewing the claims of UNM's '418 application since, that Examiner had already explicitly determined that UNM's claims were not directed toward patentably distinct subject matter.

IX. FUNDAMENTAL UNFAIRNESS

Failure to declare the requested interference would be fundamentally unfair to Fordham. By its actions (prosecution of the '418 application that issued as the '608 patent) and

omissions (UNM never informed the Examiner of pending Interference 104,761), UNM circumvented Rule 658 and obtained a patent with claims to which UNM was not entitled. Consequently, Fordham may eventually be forced into litigation with UNM in connection with a patent that should never have been allowed to issue. Moreover, should that occur, Fordham would be further prejudiced in light of the fact that the courts have not yet accepted interference estoppel as a basis for invalidating a patent.

According to the Federal Circuit, interference estoppel "has no applicability outside of internal PTO procedures" (*Exxon Corp. v. Phillips Petroleum Co.* 265 F.3d 1249, 1253, 60 USPQ2d 1368, 1371 (Fed. Cir. 2001). Notwithstanding the Court's observation that the nature of the "irregularity" was not clear to them, the Federal Circuit nevertheless observed that no court has held that interference estoppel as a ground for invalidating a patent (*Exxon* at 1254). The Federal Circuit distinguished *In re Deckler* 977 F.2d 1449 (Fed. Cir. 1992) and *In re Kroekel* 803 F.2d 705 (Fed. Cir. 1986) (discussed above) as relating to "prosecution within the PTO, not to the validity of an issued patent containing subject matter found to be patentable," and by stating that neither decision held "that a possibly imperfect interference procedure is a defense against an infringement action, whether the imperfection was due to the examiner, the applicant, or both." (*Exxon Corp. v. Phillips Petroleum Co.* 265 F.3d 1249, 1254, 60 USPQ2d 1368, 1371 (Fed. Cir. 2001). The Federal Circuit therefore affirmed the lower court's decision striking the defense of interference estoppel, indicating that "[a]bsent proof of inequitable conduct, the examiner's or the applicant's absolute compliance with the internal rules of patent examination becomes irrelevant after the patent has issued" (*Magnivision, Inc. v. Bonneau Co.* 115 F.3d 956, 960, 42 USPQ2d 1925, 1929 (Fed. Cir. 1997)) *Exxon Corp. v. Phillips Petroleum Co.* 265 F.3d 1249, 1254, 60 USPQ2d 1368, 1371 (Fed. Cir. 2001)).

Therefore, despite the final decision of the Board in Interference 104,761, Fordham may nevertheless eventually be forced to prove by clear and convincing evidence that UNM's prosecution of the '418 application leading to the '608 patent involved inequitable conduct, which includes, as one element, an intent to mislead the PTO (*FMC Corporation v. Manitowoc Company, Inc.* 835 F.2d 1411, 1415, 5 USPQ2d 1112, 1115 (Fed. Cir. 1987)). In this instance, the Board's final decision would therefore not have had any practical effect on the losing party, UNM, and, accordingly the proceedings in Interference 104,761 would be irrelevant.

X. COMPLIANCE WITH 35 U.S.C. § 135(b)

The provision of 35 U.S.C. § 135(b) does not bar declaration of the requested interference because Fordham's claims in the above-captioned application were deemed allowable prior to October 12, 2001, the date upon which Interference 104,761 was declared, which date is more than two years prior to the March 30, 2004, date upon which UNM's '608 patent issued.

CONCLUSION

Fordham respectfully requests declaration of an interference between UNM's '608 patent and the above-captioned application for the subject matter of Fordham's proposed counts 1, 2, and 3.

The proposed claim designations should be as follows:

Count 1:
Claim 1 of UNM's '608 patent
Claims 60, 62, 63, 64, 78, 89, 90, and 92 of Fordham's above-captioned application

Count 2:
Claim 2 of UNM's '608 patent
Claims 65, 66, 67, 79, 80, and 93 of Fordham's above-captioned application.

Count 3:
Claim 3 of UNM's '608 patent
Claims 68, 69, 71-75, 82-88, 94, and 95 of Fordham's above-captioned application.

Fordham should be named as senior party since Fordham has disclosed a constructive reduction to practice within the scope of the interfering subject matter as of the September 13, 1995 filing date of Fordham's '391 application, that is prior to UNM's effective filing date, September 20, 1996.

In addition, Fordham has shown that claims 1-3 of the '608 patent are unpatentable to UNM (1) pursuant to the final judgment in Interference 104,761; (2) under 35 U.S.C. § 112, first and second paragraphs; (3) under the provisions of former 37 C.F.R. § 1.658(c) as well as new 37 C.F.R. § 41.127(a) regarding interference estoppel; and (4) for UNM's inequitable conduct during prosecution of the '418 application that issued as UNM's

'608 patent. Moreover, because none of the claims of the '608 patent are, in fact, patentable to UNM, party Fordham is *prima facie* entitled to judgment over the '608 patent and an interference should be declared.

Applicant requests that the REQUEST UNDER 37 C.F.R. § 41.202(a) FOR INTERFERENCE WITH PATENT NO. 6,713,608 B2 be made of record in the file of the above-identified patent application.

Applicant believes that no fee is due for this submission. However, if a fee is due, please charge the required amount to Jones Day Deposit Account No. 50-3013.

Respectfully submitted,

Date: April 27, 2005

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Appendix A

Fordham Proposed Count 1:

A method for purifying heat shock protein complexes comprising the steps of:

adding a heat shock protein complex comprising a heat shock protein associated with at least one member of the group consisting of peptides, polypeptides, denatured proteins and antigens associated therewith to an ADP matrix column containing an ADP matrix to bind the heat shock protein complexes to the ADP matrix; and

adding a buffer containing ADP to the column to remove the heat shock protein complexes in an elution product;

wherein the heat shock protein is selected from the group consisting of hsp60, hsp65, rubisco binding protein, TCP-1, GroEL/GroES, Mif4, TCPalpha, TCPbeta, hsp104, hsp105, hsp110, DnaK, Ssa, Ssb, Ssc, hsp70, Grp75, Grp78(BiP), hsp90, gp96, and grp94.

OR

Claim 62 of Fordham's above-captioned '754 application (Alternative Count 1 of Interference 104,761):

A method for purifying heat shock protein 70 complexes comprising the steps of:

adding a solution containing a heat shock protein 70 complex comprising a heat shock protein 70 associated with at least on member of the group consisting of peptides and proteins, to an ADP matrix column containing an ADP matrix to bind the heat shock protein 70 complexes to the ADP matrix; and

adding a buffer containing ADP to the column to remove the heat shock protein 70 complexes in an elution product.

UNM's '608 Patent Claim 1 Corresponding to Fordham Proposed Count 1:	**Fordham Claim 62 Corresponding to Fordham Proposed Count 1**
1. A method for purifying heat shock protein	62. A method for purifying heat shock protein

complexes comprising the steps of: adding a solution containing heat shock protein associated with at least one member of the group consisting of peptides, polypeptides, denatured proteins and antigens to an ADP matrix column containing an ADP matrix to bind the heat shock proteins complexes to the ADP matrix; and adding a buffer containing ADP to the column to remove the heat shock protein complexes in an elution product, wherein said heat shock protein complexes are non-hsp70 heat shock protein complexes.	70 complexes comprising the steps of: adding a solution containing a heat shock protein 70 complex comprising a heat shock protein 70 associated with at least one member of the group consisting of peptides and proteins, to an ADP matrix column containing an ADP matrix to bind the heat shock protein 70 complexes to the ADP matrix; and adding a buffer containing ADP to the column to remove the heat shock protein 70 complexes in an elution product.
Fordham's Additional Allowed Claims Corresponding to Fordham Proposed Count 1:	
60. A method of purifying heat shock protein-70 peptide complexes from a cell comprising: (a) homogenizing the cell with a hypotonic buffer solution to produce a cell lysate; (b) centrifuging the cell lysate to obtain a supernatant; (c) running the supernatant over an ADP-agarose column; (d) washing the ADP-agarose column with a buffer containing ADP; and (e) collecting the heat shock protein 70-peptide complexes.	
63. The method of Claim 62 wherein the solution containing heat shock protein 70 complexes comprises a cell lysate.	
64. The method of Claim 62 wherein the heat shock protein 70 complexes comprise complexes in which the heat shock protein 70 comprises one of the group consisting of DnaK proteins from prokaryotes; Ssa, Ssb, and Ssc from yeast; hsp70, Grp75 and BiP(Grp78) from eukaryotes.	
78. The method of claim 62, wherein said member is a peptide.	

89. The method of claim 62, wherein said member is a protein, wherein the heat shock protein 70 complex comprises a heat shock protein 70 associated with a protein, and wherein the heat shock protein 70-protein complex is made in vitro.
90. The method of Claim 60, wherein the heat shock protein-70 peptide complexes comprise complexes in which the heat shock protein 70 is selected from the group consisting of a DnaK protein from a prokaryote; and hsp70(p73), hsc70(p72), and BiP(Grp78) from a eukaryote.
92. The method of Claim 62 wherein the heat shock protein 70 complexes include complexes in which the heat shock protein 70 comprises one of the group consisting of a DnaK protein from a prokaryote; and hsp70(p73), hsc70(p72), and BiP(Grp78) from a eukaryote.

Appendix B

Fordham Proposed Count 2:

A method for synthesizing heat shock protein complexes comprising the steps of:

adding a solution containing a heat shock protein to an ADP matrix column containing an ADP matrix to bind the heat shock protein to the ADP matrix;

adding a complexing solution comprising a complexing agent selected from the group consisting of peptides, polypeptides, denatured proteins and antigens to the column to form a heat shock protein complex with the heat shock protein bound to the ADP matrix column; and

adding a buffer containing ADP to the column to remove the heat shock protein complex in an elution product;

wherein the heat shock protein is selected from the group consisting of hsp60, hsp65, rubisco binding protein, TCP-1, GroEL/GroES, Mif4, TCPalpha, TCPbeta, hsp104, hsp105, hsp110, DnaK, Ssa, Ssb, Ssc, hsp70, Grp75, Grp78(BiP), hsp90, gp96, and grp94.

OR

Claim 65 of Fordham's above-captioned application, as modified to recite the following (Alternative Count 4 of Interference 104,761):

A method of synthesizing heat shock protein 70 complexes, comprising contacting a heat shock protein 70 with an antigenic molecule selected from the group consisting of peptides and proteins, and with a buffer containing ADP to allow the heat shock protein 70 to bind the antigenic molecule and to allow the heat shock protein 70 to bind to the ADP to form a heat shock protein 70 complex.

UNM's '608 Patent Claim 2 Corresponding to Fordham Proposed Count 2:	**Fordham Claim 65 Corresponding to Fordham Proposed Count 2**
2. A method for synthesizing heat shock protein complexes comprising the steps of:	65. A method for synthesizing heat shock protein 70 complexes, comprising

adding a solution containing a heat shock protein to an ADP matrix column containing an ADP matrix to bind the heat shock protein to the ADP matrix; adding a complexing solution comprising a complexing agent selected from the group consisting of peptides, polypeptides, denatured proteins and antigens to the column, to form heat shock protein complexes with the heat shock protein with the heat shock protein bound to the ADP matrix column; and adding a buffer containing ADP to the column to remove the heat shock protein complexes in an elution product, wherein said heat shock protein complexes are non-hsp70 heat shock protein complexes.	adding a heat shock protein 70 and an antigenic molecule selected from the group consisting of peptides and proteins, to a buffer containing ADP to allow the heat shock protein 70 to bind to the antigenic molecule and ADP to form a heat shock protein 70 complex.
Fordham's Additional Allowed Claims Corresponding to Fordham Proposed Count 2:	
66. The method of Claim 65, wherein the solution containing the heat shock protein 70, antigenic molecule and ADP is incubated at 37° C to induce heat shock protein 70 present in the solution to bind to peptides and proteins present in the solution to form heat shock protein 70 complexes.	
67. The method of Claim 65, wherein the heat shock protein 70 comprises one of the group consisting of DnaK proteins from prokaryotes; Ssa, Ssb, and Ssc from yeast; hsp70, Grp75 and BiP(Grp78) from eukaryotes.	
79. The method of claim 65, wherein the antigenic molecule is a peptide.	
80. The method of Claim 65, wherein the antigenic molecule is a peptide, and wherein the solution containing the heat shock protein 70, peptide and ADP is incubated at 37°C to induce	

heat shock protein 70 present in the solution to bind to the peptide present in the solution to form heat shock protein 70-peptide complexes.
93. The method of Claim 65, wherein the heat shock protein 70 comprises one of the group consisting of a DnaK protein from a prokaryote; and hsp70(p73), hsc70(p72), and BiP(Grp78) from a eukaryote.

Appendix C

Fordham Proposed Count 3:

An ADP-heat shock protein-peptide complex in purified form, wherein the heat shock protein is selected from the group consisting of DnaK, Ssa, Ssb, Ssc, hsp70, Grp75, Grp78(BiP), hsp90, gp96, and grp94.

OR

Claim 68 of Fordham's above-captioned '754 application:

An ADP-heat shock protein 70-peptide complex in substantially purified form as indicated by apparent homogeneity upon electrophoresis in a polyacrylamide gel.

UNM's '608 Patent Claim 3 Corresponding to Fordham Proposed Count 3	**Fordham Claim 68 Corresponding to Fordham Proposed Count 3**
3. An ADP-heat shock protein-peptide complex in purified form, wherein said heat shock protein complex is a non-hsp70 heat shock protein complex.	68. An ADP-heat shock protein 70-peptide complex in substantially purified form as indicated by apparent homogeneity upon electrophoresis in a polyacrylamide gel.
Fordham's Additional Allowed Claims Corresponding to Fordham Proposed Count 3:	
69. The ADP-heat shock protein 70-peptide complex of Claim 68, wherein said heat shock protein 70 comprises one of the group consisting of DnaK proteins from prokaryotes; Ssa, Ssb, and Ssc from yeast; hsp70, Grp75 and BiP(Grp78) from eukaryotes.	
71. The ADP-heat shock protein 70-peptide complex of Claim 68, wherein said ADP-heat shock protein 70-peptide complex comprises a heat shock protein70-peptide complex made *in vitro*.	
72. The ADP-heat shock protein 70-peptide complex of Claim 71, wherein said heat shock	

protein 70-peptide complex comprises a heat shock protein 70 and a peptide from the same individual.
73. The ADP-heat shock protein 70-peptide complex of Claim 71, wherein said heat shock protein 70-peptide complex comprises a heat shock protein 70 from a first individual and a peptide from a second, different individual.
74. The ADP-heat shock protein 70-peptide complex of Claim 71, wherein said heat shock protein 70-peptide complex comprises a heat shock protein 70 from a first organism and a peptide from a second, different organism.
75. The ADP-heat shock protein 70-peptide complex of Claim 71, wherein said heat shock protein 70-peptide complex comprises a heat shock protein 70 from a first species and a peptide from a second, different species.
82. An ADP-heat shock protein 70-protein complex in substantially purified form as indicated by apparent homogeneity upon electrophoresis in a polyacrylamide gel.
83. The ADP-heat shock protein 70-protein complex of Claim 82, wherein said heat shock protein 70 comprises one of the group consisting of DnaK proteins from prokaryotes; Ssa, Ssb, and Ssc from yeast; hsp70, Grp75 and BiP(Grp78) from eukaryotes.
84. The ADP-heat shock protein 70-protein complex of Claim 83, wherein said ADP-heat shock protein 70-protein complex comprises a heat shock protein70-protein complex made in vitro.
85 The ADP-heat shock protein 70-protein complex of Claim 84, wherein said heat shock protein 70-protein complex comprises a heat shock protein 70 and a protein from the same individual.
86. The ADP-heat shock protein 70-protein complex of Claim 84, wherein said heat shock protein 70-protein complex comprises a heat shock protein 70 from a first individual and a protein from a second, different individual.
87. The ADP-heat shock protein 70-protein complex of Claim 84, wherein said heat shock protein 70-protein complex comprises a heat shock protein 70 from a first organism and a protein

from a second, different organism.
88. The ADP-heat shock protein 70-protein complex of Claim 84, wherein said heat shock protein 70-protein complex comprises a heat shock protein 70 from a first species and a protein from a second, different species.
94. The ADP-heat shock protein 70-peptide complex of Claim 68, wherein said heat shock protein 70 comprises one of the group consisting of DnaK protein from a prokaryote; and hsp70(p73), hsc70(p72), and BiP(Grp78) from a eukaryote.
95. The ADP-heat shock protein 70-peptide complex of Claim 82, wherein said heat shock protein 70 comprises one of the group consisting of DnaK protein from a prokaryote; and hsp70(p73), hsc70(p72), and BiP(Grp78) from a eukaryote.

Appendix D

Fordham notes that in Interference 104,761, the Board found that Fordham's parent '391 application disclosed an embodiment falling within the scope of each of the three counts of that interference and, therefore, concluded that, for all three counts, Fordham was entitled to benefit of the September 13, 1995 filing date of its parent '391 application (Exhibit 18, pages 30-39: Section B "Fordham's entitlement to the benefit of its 391 application"). As noted above (*see* Section III), Fordham Proposed Counts 1-3, are analogous to, or broader than, Count 1, 4(2), and 3 of Interference 104,761 respectively (*see* Appendix E, below, which compares Counts 1, 4(2), and 3 of Interference 104,761 with Fordham Proposed Counts 1-3).

Accordingly, it follows that Fordham's parent '391 application as well as its above-identified '754 application (a continuation of the '391 application) have both described, in a 35 U.S.C. § 112 compliant manner, a constructive reduction to practice that falls within the scope of each of Fordham Proposed Counts 1, 2, and 3.

Notwithstanding the above, in order to comply with Board Rule 202(a)(6), Fordham also provides the information below.

Fordham Proposed Count 1:

Support for a constructive reduction to practice falling within the scope of the interfering subject matter defined by Fordham Proposed Count 1 is found both in Fordham's parent '391 application as well as in Fordham's above-captioned '754 application, which is a division of Fordham's '391 application.

Specifically, support for purification of hsp70-peptide complexes using an ADP-agarose column is found at page 60, lines 5-25, and at page 25, lines 1-17 of both Fordham's '391 parent application (Exhibit 22) Fordham's above-identified pending '754 application (Exhibit 9).

Fordham Proposed Count 2:

Support for a constructive reduction to practice falling within the scope of the interfering subject matter defined by Fordham Proposed Count 2 is found both in Fordham's parent '391 application as well as in Fordham's above-captioned '754 application, which is a division of Fordham's '391 application.

Specifically, support for the synthesis of hsp70-peptide complexes involving the co-incubation of purified hsp70, an antigenic molecule, and ADP, is found at page 36, lines 25-32 of both Fordham's parent '391 application (Exhibit 22) and Fordham's above-identified pending '754 application (Exhibit 9).

Fordham Proposed Count 3:

Support for a constructive reduction to practice within the scope of the interfering subject matter defined by Fordham Proposed Count 3 is found both in Fordham's parent '391 application as well as in Fordham's above-captioned '754 application, which is a division of Fordham's '391 application.

The method of purification of hsp70-peptide complexes (disclosed at page 60, lines 5-25 and at page 25, lines 1-17 of both Fordham's parent '391 application (Exhibit 22) and Fordham's above-identified '754 application (Exhibit 9)) and the method of synthesis of hsp70-peptide (disclosed at page 36, lines 25-32 of both Fordham's parent '391 application (Exhibit 22) and Fordham's above-identified pending '754 application (Exhibit 9)) both inherently produce hsp70-ADP-peptide complexes; (*also see* Exhibit 9 and Exhibit 22 at page 60, lines 19-21).

Additional support for an embodiment falling within the scope of Fordham Proposed Count 3 is found in the Preliminary Amendment filed January 13, 1999, in connection with Fordham's above-identified, pending '754 application. This preliminary amendment did not introduce new matter and was entered by the Examiner (Exhibit 21, at page 12 third paragraph; at page 10, first full paragraph; and at page 11, first paragraph).

The preliminary amendment filed in connection with Fordham's above-identified pending '754 application amended the specification at page 16, line 25, by actually incorporating material that had been incorporated by reference in Fordham's earlier-filed parent '391 application (Exhibit 21, at page 11, second full paragraph through and including the first two paragraphs of page 12; and at page 3, line 1 through line 2 at page 4). This preliminary amendment (Exhibit 21) also amended the specification at page 36, line 31, and at page 60, line 22, to recite an inherent property of the complex produced by the methods described at page 36, lines 25-32, and at page 60, line 5-25, respectively (Exhibit 21, at page 12, third paragraph, at page 4, lines 18-19, and at page 6, lines 5-7).

Appendix E

Comparison of Counts 1, 4(2), and 3 of Interference 104,761 To Fordham Proposed Counts 1, 2, and 3

Count 1 of Interference 104,761 Count 1 of Interference 104,761 was defined as the method of claim 10 of UNM's '332 Patent OR Fordham Claim 62	**Fordham Proposed Count 1**
The method of claim 1 [A method for purifying heat shock protein complexes comprising the steps of: adding a heat shock protein complex comprising a heat shock protein associated with at least one member of the group consisting of peptides, polypeptides, denatured proteins and antigens associated therewith to ADP matrix column containing an ADP matrix to bind the heat shock protein complexes to the ADP matrix; and adding a buffer containing ADP to the column to remove the heat shock protein complexes in an elution product.] wherein the heat shock protein complexes include complexes in which the heat shock protein comprises one of the group consisting of DnaK proteins from prokaryotes; Ssa, Ssb, and Ssc from yeast; hsp70, Grp75 and Grp78 (Bip) from eukaryotes.	A method for purifying heat shock protein complexes comprising the steps of: adding a heat shock protein complex comprising a heat shock protein associated with at least one member of the group consisting of peptides, polypeptides, denatured proteins and antigens to an ADP matrix column containing an ADP matrix to bind the heat shock protein complexes to the ADP matrix; and adding a buffer containing ADP to the column to remove the heat shock protein complexes in an elution product; wherein the heat shock protein is selected from the group consisting of hsp60, hsp65, rubisco binding protein, TCP-1, GroEL/GroES, Mif4, TCPalpha, TCPbeta, hsp104, hsp105, hsp110, DnaK, Ssa, Ssb, Ssc, hsp70, Grp75, Grp78(BiP), hsp90, gp96, and grp94.
OR	**OR**

Fordham Claim 62: A method for purifying heat shock protein 70 complexes, comprising the steps of: adding a solution containing a heat shock protein 70 complex comprising a heat shock protein 70 associated with at least one member of the group consisting of peptides and proteins, to an ADP matrix column containing and ADP matrix to bind the heat shock protein 70 complexes to the ADP matrix; and adding a buffer containing ADP to the column to remove the heat shock protein 70 complexes in an elution product.	Fordham Claim 62: A method for purifying heat shock protein 70 complexes comprising the steps of: adding a solution containing a heat shock protein 70 complex comprising a heat shock protein 70 associated with at least on member of the group consisting of peptides and proteins, to an ADP matrix column containing an ADP matrix to bind the heat shock protein 70 complexes to the ADP matrix; and adding a buffer containing ADP to the column to remove the heat shock protein 70 complexes in an elution product.

Count 4(2) of Interference 104,761	**Fordham Proposed Count 2**
Count 4(2) of Interference 104,761 was defined as the method of claim 22 of UNM's '332 patent OR as Fordham proposed claim 96, a modification of Fordham claim 65.	
The method of claim 13 [A method for synthesizing heat shock protein complexes comprising the steps of: adding a heat shock protein to an ADP matrix column to bind the heat shock protein; adding a complexing solution comprising a complexing agent selected from the group consisting of peptides, polypeptides, denatured	A method for synthesizing heat shock protein complexes comprising the steps of: adding a solution containing a heat shock protein to an ADP matrix column containing an ADP matrix to bind the heat shock protein to the ADP matrix; adding a complexing solution comprising a complexing agent selected from the group consisting of peptides, polypeptides, denatured

proteins and antigens to the column to form a heat shock protein complex with the heat shock protein bound to the ADP matrix column; and adding a buffer containing ADP to the column to remove the heat shock protein complex in an elution product] wherein the heat shock protein complexes include complexes in which the heat shock protein comprises one of the group consisting of DnaK proteins from prokaryotes; Ssa, Ssb, and Ssc from yeast; hsp70, Grp75 and Grp78(Bip) from eukaryotes.	proteins and antigens to the column to form a heat shock protein complex with the heat shock protein bound to the ADP matrix column; and adding a buffer containing ADP to the column to remove the heat shock protein complex in an elution product; wherein the heat shock protein is selected from the group consisting of hsp60, hsp65, rubisco binding protein, TCP-1, GroEL/GroES, Mif4, TCPalpha, TCPbeta, hsp104, hsp105, hsp110, DnaK, Ssa, Ssb, Ssc, hsp70, Grp75, Grp78(BiP), hsp90, gp96, and grp94.
OR	**OR**
A method of synthesizing heat shock protein 70 complexes, comprising contacting a heat shock protein 70 with an antigenic molecule selected from the group consisting of peptides and proteins, and with a buffer containing ADP to allow the heat shock protein 70 to bind the antigenic molecule and to allow the heat shock protein 70 to bind to the ADP to form a heat shock protein 70 complex.	A method of synthesizing heat shock protein 70 complexes, comprising contacting a heat shock protein 70 with an antigenic molecule selected from the group consisting of peptides and proteins, and with a buffer containing ADP to allow the heat shock protein 70 to bind the antigenic molecule and to allow the heat shock protein 70 to bind to the ADP to form a heat shock protein 70 complex.

Count 3 of Interference 104,761	**Fordham Proposed Count 3**
Count 3 of Interference 104,761 is the ADP-heat shock protein-peptide complex of claims 13, 19, or 25 of UNM's '716 patent	
13. A purified ADP-heat shock protein-peptide complex, wherein said heat	An ADP-heat shock protein-peptide complex in purified form, wherein the heat shock

shock protein is selected from the group consisting of DnaK proteins from prokaryotes. 19. A purified ADP-heat shock protein-peptide complex, wherein said heat shock protein is selected from the group consisting of Ssa, Ssb, and Ssc from yeast. 25. A purified ADP-heat shock protein-peptide complex, wherein said heat shock protein is selected from the group consisting of Grp75 and Grp78(Bip) from eukaryotes.	protein is selected from the group consisting of DnaK, Ssa, Ssb, Ssc, hsp70, Grp75, Grp78(BiP), hsp90, gp96, and grp94. **OR** Fordham Claim 68: An ADP-heat shock protein 70-peptide complex in substantially purified form as indicated by apparent homogeneity upon electrophoresis in a polyacrylamide gel.